*Kirk-Othmer Encyclopedia of Chemical Technology.*


# INDUSTRIAL ANTIMICROBIAL AGENTS

Industrial antimicrobial agents are chemicals used to prevent the adverse consequences of microbiological activity in processes and products. Some are unique to this segment and others are drawn from the antimicrobial agents used in medicine, agriculture, and sanitary applications. Industrial antimicrobials are selected where process or strictly physical conditions, such as irradiation or heat, are impractical or ineffective in controlling microbiological activity.

Microorganisms are ubiquitous, thus microbial contamination is the rule; the total absence of microbes, ie, sterility, is the exception. Many microorganisms might be considered mainstream, growing under typical ambient conditions, but there are almost always strains that are capable of surviving and multiplying under the extremes of pH, salinity, pressure, and temperature.

Chemical suppliers include basic manufacturers of active ingredients, formulators, and distribution or service industries. The relative importance of each depends greatly upon the industry being supplied. In many instances, the vendor may supply a number of performance chemicals (eg, corrosion control agents or stabilizers) in addition to the antimicrobial agent.

## 1. Microbiology

Industrial antimicrobial agents are targeted against bacteria, mold, and fungi. Bacteria are simple, single-celled organisms that are rarely over two to three micrometers in size. The identification of a microorganism is based on its size, shape, biochemical activity, and growth characteristics. More recently, the fields of serology and DNA homology have contributed to rapid and simplified bacterial identification.

Fungi are somewhat more complex than bacteria and more similar in physiology to the higher organisms. This similarity, unfortunately, makes discovery of biocides that specifically block fungal growth, with no effects harmful to humans, much more difficult. Fungal cells typically differentiate so that not all of the cells making up the organism are the same, which is not true of bacteria. Fungi readily grow into a size easily visible to the unaided eye.

Yeasts and algae are also microorganisms that fall within the category of targets of industrial antimicrobial agents. Algae, of course, are photosynthetic, that is, they convert light into chemical energy. Yeasts are similar to fungi in physiology, but are unicellular like bacteria.

All organisms require a source of energy, nitrogen for nucleic acid and amino acid synthesis, and essential nutrients such as phosphorus, sulfur, magnesium, and water. Microorganisms display a tremendous range in their requirements for nutrients. Fastidious organisms require specific forms of certain nutrients, such as amino acids or vitamins. Organisms causing problems in industrial situations are frequently at the opposite end of the spectrum, being extremely self-sufficient in synthesizing required biochemicals from the most basic molecules. The type and availability of nutrient may be the most significant determinant in the microbiological ecology of the products and processes which require the use of an industrial antimicrobial agent.

Viruses are obligate intracellular parasites. They only exhibit activity by infecting other living organisms, thus they are not a practical concern in industrial microbiological fields. The exception is where viral contamination of the product or process represents a threat of transmission of disease. Microscopic insects and protozoans are also not addressed in this article (see Insect control technology).

There are about 30,000 species of bacteria (1), which, by historical convention, are placed into gram-positive or gram-negative groups (after Hans Gram, a turn-of-the-century Danish researcher), based on the bacterial affinity for staining with a dye (2). Both gram-positive and gram-negative organisms are problematic in a number of industrial situations. They display some distinctiveness in their individual responses to antimicrobial agents.

## 2. Antimicrobial Activity

Microbiologists have developed the following hierarchy to categorize the expected level of performance of antimicrobial treatments:

| Category | Result of treatment |
|---|---|
| sterilant | completely kills all life forms |
| sporicidal | kills spores |
| disinfectant | kills all infectious bacteria |
| cidal | kills all organisms of type (eg, tuberculocidal) |
| sanitizer | reduces number of organisms to safe level |
| antiseptic | prevents infection |
| static | prevents growth of organism (eg, fungistatic) |

Some chemicals function by killing microorganisms (3, 4), whereas others merely prevent organisms from growing or reproducing. Frequently biocide chemicals with a high degree of cidal activity are reactive. Clearly, if the reactivity is not specifically targeted toward biochemicals essential to the microorganisms in the system, the biocide may be consumed in the application and rendered ineffective. Biocide chemicals limited to a static level are typically less reactive and exhibit a longer span of functionality. Thus, cidal activity is not necessarily preferred to static activity. The selection of biocide chemistry is a balance between reactivity and stability, which must be attuned to the requirements of the industrial application. A more extensive survey of the nomenclature associated with levels of microbiological control has been provided (5) (see Disinfectants and antiseptics).

### 2.1. Measures of Activity

The potency of an antimicrobial to kill or render the organisms inactive is measured by the minimum inhibitory concentration (MIC). This property is obtained in a laboratory test in which the test compound is added at stepwise concentrations to microbiological media, followed by inoculation with a pure culture of microorganism. In the absence of growth, the media are unchanged. If growth occurs, the media appear turbid due to the high population of the bacteria. The lowest concentration inhibiting growth is the MIC for that organism (the lower the number, the more potent the antimicrobial). MICs are widely available, but minor differences in protocol result in some reported differences. The MIC is of little value to the users of antimicrobials because it is not a true predictor of performance in any particular application, and more application-specific tests have been developed.

| Process uses | Preservative uses |
|---|---|
| Swimming pool sanitizers | |
| Cooling water | |
| Metalworking | |
| Pigment slurries | |
| Petroleum recovery | Jet fuel |
| Pulp | Paper |
| Paint (in-can) | Paint film |
| Latex | Caulks |
| Adhesive | Adhesives |
| Hide processing | Leather |
| Sapstain | Wood |
| Laundry sanitizers | Textile |
| | Plastics |
| | Cosmetics |

**Fig. 1.** Applications of industrial antimicrobial agents.

## 3. Applications

Practically, the broad general area of industrial antimicrobial concerns is divided into process and preservative disciplines. Figure 1 shows the key application areas of process and companion-preservative uses, and Table 1 indicates the various market segments.

**Table 1. Value of U.S. Antimicrobial Industrial Agent Markets**

| Market segment | Value, $10^6$ $ |
|---|---|
| wood/sapstain | 200 |
| swimming pool sanitizers | 200 |
| paints/coatings | 50-100 |
| cooling water | 20–50 |
| metalworking | 20–50 |
| pulp/paper | 20–50 |
| plastics | 20–50 |
| adhesives | 2–20 |
| petroleum/fuel | 2–20 |
| slurries | 2–20 |
| latex/caulk | 2–20 |
| laundry textile | 2–20 |
| hides/leather | 2–20 |

It is common to consider the preservative use a service-life challenge which may require several years for successful performance, whereas the process uses are of limited duration. On the other hand, some processes are ongoing operations which require regular treatment with antimicrobials. The commonality running throughout the various processes is the presence of significant amounts of water. Both bacteria and fungi can flourish in aqueous systems; fungi are most notably the problem when liquid moisture is less available, as might be encountered during the service life of the products listed as preservatives in Figure 1.

Efficiency testing needs to be conducted with actual conditions simulated as closely as possible (3, 6, 7). Table 2 presents some of the standardized protocols available to microbiology labs for confirmation of usefulness (8).

**Table 2. Common Test Methods for Evaluating Materials[a]**

| Material | Method | Organism | Result |
|---|---|---|---|
| adhesives | ASTM D1174 | mixed bacterial culture | bacterial growth, viscosity change |
| | ASTM D4300 | mixed fungi | growth on film |
| | ASTM D1286 | mixed fungal culture | fungal growth, viscosity change |
| metalworking fluid | ASTM E686 | fungal and bacterial mixed culture | organism growth, physical change |
| | ASTM D3946 | spoiled material | organism growth, physical change |
| paint | ASTM D2574 | bacterial culture | bacterial growth |
| | ASTM D3273 | mixed fungal culture | surface growth |
| paper | UL181 | fungal culture | surface growth |
| | ASTM D2020 | mixed fungal culture | surface growth |
| | TAPPI T487, M54 | mixed fungal culture | surface growth |
| plastic | ASTM G21 | mixed fungal culture | surface growth |
| | ASTM G22 | *Pseudomonas aeruginosa* | visible growth |
| | ASTM G29 | freshwater algae | algal attachment |
| | ASTM D3083 | soil burial | staining, weight loss, stiffness |
| textile | AATCC Method 90 | bacterial cultures | zone of inhibition |
| | AATCC Method 100 | bacterial cultures | percent reduction |
| wood | ASTM D2017 | fungal enriched soil burial | weight loss |
| | ASTM D1413 | fungal enriched soil burial | weight loss, decay |

[a]Ref. 8

## 4. Regulation of Antimicrobial Agents

The key trend affecting this industry is the regulation of products and their uses by the U.S. Environmental Protection Agency (EPA). This regulation has curtailed the introduction of new ingredients, selectively limited the markets for a number of products, and eliminated products by suspension or cancellation. The data in Figure 2 show the number of approvals by the EPA made for new industrial antimicrobials since the early 1970s (9). During this same period, the total number of new active ingredients (eg, insecticides, agricultural fungicides, and herbicides) has averaged between 12 and 13 approvals per year. The hallmark of approval is a registration.

Several antimicrobials have been banned or severely restricted by the EPA based on documented or suspected toxicity or environmental problems. Others have been discontinued in the face of testing costs required by the EPA reregistration program mandated by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1988 (10). Some of the significant products that have become obsolete are 2,4,5-trichlorophenol[95-95-4], sodium 2,4,5-trichlorophenate[136-32-3], hexachlorophene[70-30-4], 2,2′-methylenebis(4-chlorophenol)[27-23-4], phenylmercuric acetate[62-38-4], and 3,4,5-tribromosalicylanilide[38848-67-8].

Contraction in the number of EPA-allowed biocides has heightened efforts to develop naturally derived preservatives and microorganisms capable of countering microbial degradation. Neem oil (*Azadirachta indica* seed extract) has been featured as an exceptional natural candidate for the preservation of cosmetic products. Naturally derived chemicals with antimicrobial properties have been used since antiquity as preservatives.

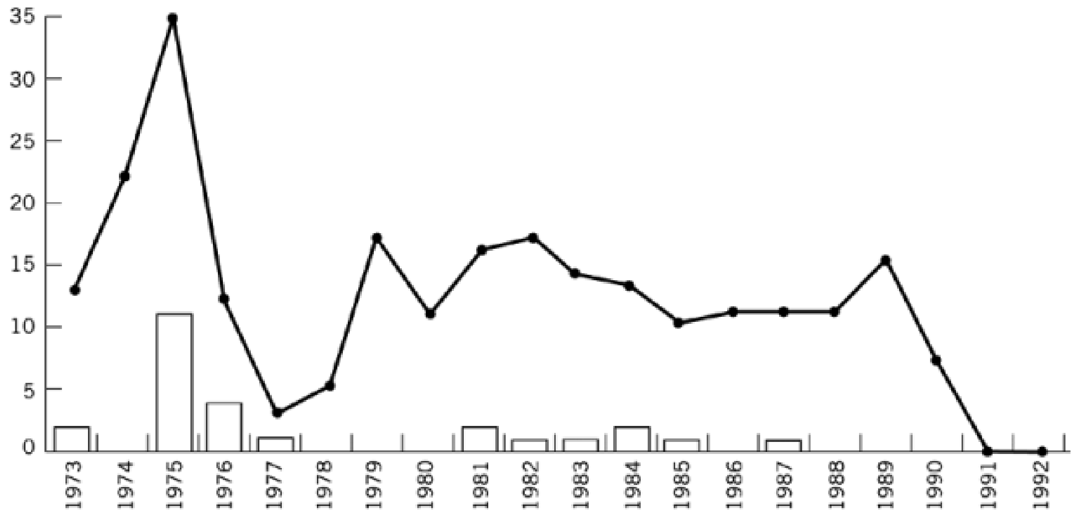



**Fig. 2.** EPA registrations issued for new active ingredients: (□), new bactericides and slimicides; (•), all pesticides.

However, displacement of successful synthetic products by natural products in preservatives of any category remains to be witnessed.

#### 4.1. Toxicology

Industrial antimicrobial agents are regulated in the United States as pesticides under FIFRA. Thus the industrial antimicrobial regulation is strongly influenced by agricultural pesticide considerations. The hallmark of the EPA allowance is registration, which is the culmination of a process that begins with the submission of toxicology, chemistry, and environmental data showing that the product can be used without "adverse effects on man and the environment." An approval to sell a product in the United States reflects a review of substantial amounts of toxicology data and a conclusion that the product can be safely used for its intended purpose.

The most often quoted toxicology data is the acute oral $LD_{50}$. This number is a crude measurement of the potential hazard to humans (and other mammals) from ingestion. Ingestion by individuals working in industrial/commercial settings is limited as a result of training programs, warnings, and industrial hygiene; therefore the $LD_{50}$ alone bears little direct relevance to the safe use of a product. Much more instructive is the documentation of quantifiable hazards associated with repeated exposure scenarios that are typical of the conditions of use (11).

The U.S. EPA regulates both the active ingredient (technical or formulating grade) and the formulated (end use) products. Data requirements for the active ingredient are much more substantial than for the formulated product. Because of the importance of toxicology studies to the development of antimicrobials, the minimum toxicology data requirements and cost estimates for studies conducted at contract laboratories are noted in Table 3 (12). This data is required for products with minimal opportunity for human exposure, Tier I (according to EPA convention). Analysis of the data obtained in the Tier I series allows a rational comparison of favorable or unfavorable toxicology of a candidate antimicrobial agent.

The cost of developing a new active ingredient, however, is much more costly than the basic costs involved in toxicology studies, as shown in Table 3, and is likely to be $\$35 \times 10^6$ (13).

**Table 3. Estimated Cost of Toxicology Study[a]**

| Study | Cost for active ingredient, $ | Cost for formulation, $ |
|---|---|---|
| | *Acute series* | |
| acute dermal $LD_{50}$ | 7, 000 | 7, 000 |
| acute inhalation $LC_{50}$ | 22, 000 | 22, 000 |
| eye irritation | 1, 250 | 1, 250 |
| skin irritation | 1, 250 | 1, 250 |
| sensitization | 10, 000 | 10, 000 |
| *subtotal* | 45, 000 | 45, 000 |
| | *Tier I[b] series* | |
| 90-day subchronic | 75, 000 | |
| teratology | 125, 000 | |
| mutagenicity | 30, 000 | |
| *subtotal* | 230, 000 | 45, 000 |
| *Total* | 275, 000 | 45, 000 |

[a]Ref. 12.
[b]EPA-defined as minimal opportunity for human exposure.

### 4.2. Reregistration

In addition to its authority to control the availability of new active ingredients, formulations, and the way in which the formulas are used, EPA is reapproving the use of older products through a process known as reregistration. In order to achieve some administrative economy, EPA has grouped some of the biocides with chemical similarity into a generic cluster known in reregistration as a case. Additionally, there are a number of active ingredient families which are being handled in a generic case. For example, the case of tributyltin- (TBT) containing compounds includes bis(tributyltin) oxide[56-35-9], bis(tributyltin) salicylate[22330-14-9], tributyltin benzoate[4342-36-3], tributyltin fluoride[1983-10-4], tributyltin maleate[14275-57-1], and tributyltin methacrylate[2155-70-6].

Because manufacturers are unwilling to generate data to substantiate the acceptability of continued use, the other tin compounds of the case have become obsolete, including bis(tributyltin) adipate[7437-35-6], bis(tributyltin) sulfosalicylate[4419-22-1], tributyltin acetate[56-36-0], tributyltin acrylate[13331-52-7], tributyltin chloride[1461-22-9], tributyltin linoleate[24124-25-2], tributyltin monopropylene glycol maleate[53466-85-6], and tributyltin neodecanoate[28801-69-6]. Because of the substantial number of tin compounds, this is not a typical example, but it does illustrate the point that there has been a large decline in the availability of niche products.

## 5. Manufacturers and Suppliers

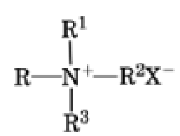
Manufacturers and suppliers of industrial antimicrobial active ingredients and formulations include the following companies:

| | |
|---|---|
| ANGUS Chemical Co.Northbrook, Ill. | Miles, Inc.Pittsburgh, Pa. |
| BASFParsippany, N.J. | Morton International, Inc.Danvers, Mass. |
| Calgon Corp.Moon Run, Pa. | Petrolite Corp.St. Louis, Mo. |
| Dearborn Division,W. R. GraceLake Zurich, Ill. | Stepan Co.Northfield, Ill. |
| Huls AmericaPiscataway, N.J. | Union Carbide ChemicalsDanbury, Conn. |
| Lonza Inc.Fairlawn, N.J. | Baker Performance ChemicalsHouston, Tex. |
| Mooney Chemical, Inc.Cleveland, Ohio | Buckman LaboratoriesMemphis, Tenn. |
| Osmose Wood Perserving Co.Buffalo, N.Y. | Dow Chemical USAMidland, Mich. |
| Rohm and Haas Co.Philadelphia, Pa. | Hickson Corp.Conley, Ga. |
| Troy Chemical Corp.Newark, N.J. | Lehn & Fink Products Co.Montvale, N.J. |
| Zeneca (formerly ICI)Wilmington, Del. | Monsanto Co.St. Louis, Mo. |
| Atochem North AmericaPhiladelphia, Pa. | Olin Corp.Cheshire, Conn. |
| Betz LaboratoriesTrevose, Pa. | Rhône-Poulenc RorerPrinceton, N.J. |
| CSICharlotte, N.C. | SherexDublin, Ohio |
| Great Lakes ChemicalsWest Lafayette, Ind. | Vinings Industries, Inc.Atlanta, Ga. |
| ISK BiotechMentor, Ohio | |

## 6. Classes of Antimicrobial Compounds

### 6.1. Quaternary Ammonium Compounds

These compounds (quats) have the following general formula:



where X = $Cl^-$ or $Br^-$

The quaternary ammonium compounds (qv) are manufactured by the reaction of an alkyl halide with a tertiary amine. The alkyl halide may be short-chain, long-chain, or benzyl. Selection of a long-chain alkyl group yields structures with variable composition and greatly adds to the chemical complexity inherent in this group. Investigation of structure-activity relationships has led to claims for superior efficacy or compatibility, most notedly with anionic surfactants in disinfectant-detergent cleaner systems, of closely related compounds in the family.

The quats are an extremely important group in medical and sanitary applications, with comparatively limited industrial applications. Activity against bacteria of public health importance is absolutely required, with a lesser demand being made for antifungal activity.

The key markets for quaternaries are as swimming pool algaecides and in cooling water applications (see Water, treatment of swimming pools, spas, and hot tubs), which further explains their importance as process biocides rather than preservatives. Some uses in latex films and plastics have been claimed (14, 15). Primary quaternary ammonium industrial antimicrobial agents and their producers are presented in Table 4.

**Table 4. Quaternary Ammonium Industrial Antimicrobial Agents**

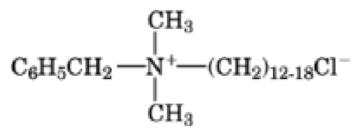
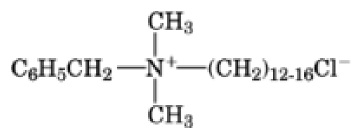
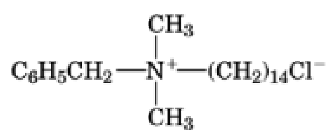
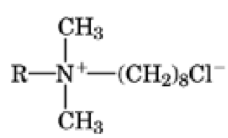
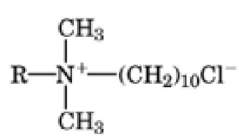
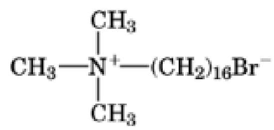
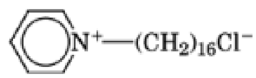
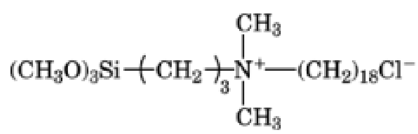
| Chemical name | CAS Registry Number | Structure | R | Trade name | Producer |
|---|---|---|---|---|---|
| benzalkonium chlorides | [68391-01-5] |  | $(C_{12--18}\ H_2)$ | Variquat | Huntington |
| | [68424-85-1] |  | $(C_{12--16}\ H_2)$ | BTC | Lonza |
| | [139-08-2] |  | $(C_{14}\ H_2)$ | | Sherex Stephan |
| dialkyldimethyl-ammonium chlorides | [5538-94-3] |  | $C_8$ | Bardac LF | Lonza/Stepan |
| | [7173-51-5] |  | $C_{10}$ | Bardac 2250 | |

**Table 4.** ***Continued***

| Chemical name | CAS Registry Number | Structure | R | Trade name | Producer |
|---|---|---|---|---|---|
| cetyltrimethyl-ammonium bromide | [57-09-0] |  | $C_{16}$ | Bardac 22 Bromat | Lonza Hexcel |
| cetylpyridinium chloride[a] | [123-03-5] |  | $C_{16}$ | | Hexcel |
| 3-(trimethoxysilyl)-propyldimethyl-octadecyl-ammonium chloride | [27668-52-6] |  | $C_{18}$ | Q-5700 Durotex QST | Dow-Corning Morton |

[a]Cetyl = hexadecyl.

The mechanism of action of quats has been widely studied. It is generally agreed that their interaction with the bacterial cell membrane is the primary event resulting in antimicrobial activity (16, 17).

Regulatory pressures which have limited the introduction of new chemistries have led to a substantial trend to obtain innovation through combination. One apparently successful introduction is the combination of a quat with a polyphase for sapstain prevention on freshly sawn lumber (18).

Quats are usually moderately soluble in water, but this varies widely owing to the range of groups bonded to the nitrogen. They are fundamentally nonreactive but act as surface–active cations. Compatibility with anionic detergents and activity in the presence of hard water have been claimed for some quats (19).

### 6.2. Phenolics

Phenol (qv) and the chlorinated phenolics formerly comprised the largest class of industrial antimicrobials (see Chlorophenols). Table 5 shows the remaining phenolics of importance. Use of pentachlorophenol has been severely restricted; only one manufacturer supplies product for the wood preservation market.

**Table 5. Phenolic Industrial Antimicrobials**

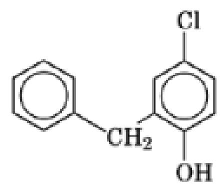
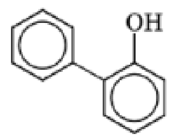
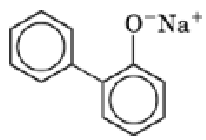
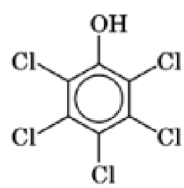
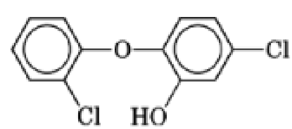
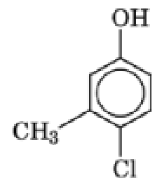
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| 2-benzyl-4-chlorophenol | [120-32-1] |  | Santophen 1 | Monsanto | disinfectants |
| *o*-phenylphenol | [90-43-7] |  | Dowicide 1 | Dow | metalworking fluids, leather, paint |
| sodium *o*-phenylphenate | [132-27-4] |  | Dowicide A | Dow | metalworking fluids, adhesives, paint, textiles |
| pentachlorophenol | [87-86-5] |  | Glazd | Vulcan | wood |
| 2(2′,4′-dichlorophenoxy)-5-chlorophenol | [3380-34-5] |  | Irgasan | CIBA-GEIGY | textiles |

**Table 5.** ***Continued***

| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| 4-chloro-3-methylphenol | [59-50-7] |  | PCMC | Hüls | adhesives, latex |

Sodium orthophenyl phenate remains an important ingredient in the treatment of cooling waters. Both orthophenyl and its sodium salt have a wide spectrum of preservative use, including caulks, construction products, and leather processing. Similarly, *para*-chloro-*meta*-xylenol is used to preserve a number of water-based goods, including inks (qv), emulsions, and shoe polish, in addition to providing mold resistance to leather.

The most common use of 2-(2′,4′-dichlorophenoxy)-5-chlorophenol (2,4,4′-trichloro 2′-phenoxyphenol) is in the personal care products market, where it is commonly known as triclosan and is the active antibacterial in underarm deodorants. It has also found some acceptance as an antibacterial component of plastic mattress covers.

### 6.3. Chlorine and Bromine Oxidizing Compounds

The organo chlorine compounds shown in Table 6 share chemistry with inorganic compounds, such as chlorine[7782-50-5] and sodium hypochlorite[7681-52-9]. The fundamental action of chlorine compounds involves hydrolysis to hypochlorous acid (see Chlorine oxygen acids and salts).

$$Cl_2 + H_2O \longrightarrow HOCl + HCl$$

$$HOCl \rightleftharpoons H^+ + OCl^-$$

The dissociation of hypochlorous acid is an equilibrium reaction and pH-dependent. The microbiological activity of chlorine and its derivatives is strongly influenced by the pH of the solution, exhibiting much greater activity at pH less than 7, leading to the conclusion that the active microbiocide is the undissociated hypochlorous acid (20). Principal halogen-containing industrial antimicrobial agents and their manufacturers and applications are listed in Table 6. Iodine compounds include *p*-tolydiiodomethyl sulfone[20018-09-1] (Amical 48), a paint mildewcide produced by Angus, and 3-iodo-2-propynylbutyl carbamate [55406-55-6] (Polyphase), used on wood and in adhesives, produced by Troy.

**Table 6. Halogen-Containing Industrial Antimicrobial Agents**

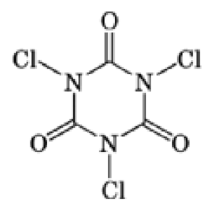
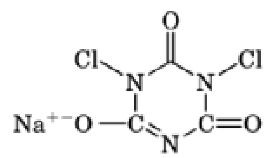
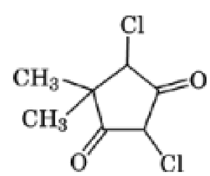
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| | | *Chlorine compounds* | | | |
| trichloroisocyanurate | [87-90-1] |  | ACL-85<br>CDB-90 Pace | Monsanto<br>FMC Olin | swimming pool sanitizer |
| sodium dichloroisocyanurate | [2893-78-9][a] |  | ACL-60<br>ACL-56<br>Clearon | Monsanto<br>Monsanto<br>FMC | swimming pool sanitizer, disinfectant |
| potassium dichloroisocyanurate | [2244-21-5] | $Na^{+-}O$ | ACL-59 | Monsanto | swimming pool sanitizer, disinfectant |
| monotrichloroisocyanurate: potassium dichloro-isocyanurate, 1:4 dichlorodimethylhydantoin | [34651-95-1][118-52-5] |  | ACL-66Halane | Monsanto<br>BASF Wyandotte | swimming pool sanitizer, disinfectant disinfectant |
| | | *Bromine compounds* | | | |
| bromochlorodimethylhydantoin | [126-06-7] | | DiHalo sticks | Great Lakes | swimming pool disinfectant |
| 2,2′-dibromo-3-nitrilopropionamide | [10222-01-2] | $N{\equiv}CCBr_2CONH_2$ | DBNPA | Dow | cooling water slimicide, secondary oil recovery metalworking fluids |

**Table 6.** ***Continued***

| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| bis(1,4-bromoacetoxy)-2-butene | [20679-58-7] | $BrCH_2COOCH_2CH$<br>$\parallel$<br>$BrCH_2COOCH_2CH$ | Slimacide V-10 | Vineland | paper-mill slimicide |
| 1,2-dibromo-2,4-dicyanobutane | [35691-65-7] | $BrCH_2CBr(CN)CH_2CH_2CN$ | Tektamer 38 | Calgon | paint, adhesive, latex emulsion, joint compound |
| 2-bromo-2-nitropropane-1,3-diol | [52-51-7] | $HOCH_2CBr(NO_2)CH_2OH$ | Bronopol | Angus | cosmetic preservative |
| benzyl bromoacetate | [5437-45-6] | $C_6H_5CH_2$—$OOCCH_2Br$ | Merbac 35 | Calgon | paint, latexes |

[a]The dihydrate has the CAS Registry Number [57580-86-0]

The organo chlorine compounds are more expensive than inorganic chlorine compounds, but offer improved stability against photolytic breakdown in swimming pools (21). Swimming pool sanitation is generally accomplished with 1–3 ppm free chlorine residual (see Chloramines and bromamines; Water, treatment of swimming pools, spas, and hot tubs).

Inorganic chlorine and organic chlorine compounds are also used in cooling water treatment. The cost of organic chlorine is offset by a greater range of pH tolerance (22). The efficacy of chlorine compounds is due to strong oxidizing capacity. However, because of the nonspecific nature of the reactivity, a significant portion of the added chemical can be lost to reaction with organic matter (eg, partially decayed chemicals of biological origin) contaminating the system. Thus it is necessary to satisfy the chlorine demand of the system (23).

In cooling water applications, great importance is placed on activity against *Legionella pneumophila*, the causative agent of Legionnaires' disease. Bromochloro dimethylhydantoin has been shown to rapidly hydrolyze in water with the formation of hypobromous acid (21). The $pK_a$ of hypobromous acid is 8.8, whereas the $pK_a$ of hypochlorous acid is 7.4. Because the undissociated hypohalous acid is the active biocide, the hypobromous-generating chemical is more active in alkaline systems.

Chlorine dioxide has substantial reactivity, which precludes its shipment in bulk. New technology that allows on-site generation of $ClO_2$ from sodium chlorate [7775-09-9] rather than from chlorine is expected to result in its more frequent use in applications where capital investment and operators are warranted (24).

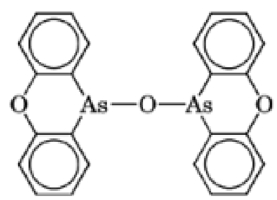
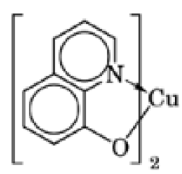
Sodium bromide is the most rapidly growing antimicrobial in water treatment applications (25). Chlorine dioxide [10049-04-4] has not been historically important, but may have a bright future because of its excellent antimicrobial activity without formation of halomethanes or chloramines (26).

Resistance to antimicrobial agents is of concern as it is well known that bacterial resistance to antibiotics can develop. Many bacteria already derive some nonspecific resistance to biocides through morphological features such as their cell wall. Bacterial populations present as part of a biofilm have achieved additional resistance owing to the more complex and thicker nature of the biofilm. A system contaminated with a biofilm population can require several orders of magnitude more chlorine to achieve control than unassociated bacteria of the same species. A second type of resistance is attributed to chemical deactivation of the biocide. This deactivation resistance to the strong oxidizing biocides probably will not occur (27).

### 6.4. Organometallics

Organometallics, listed in Table 7, were previously dominated by the mercurial compounds. For example, phenyl mercuric acetate [62-38-4] previously was a dominant mildewcide for paint (28), but was regulated out of use by EPA in 1990. Mercury compounds were preferred for their broad activity and effectiveness, both for in-can and paint-film protection, compared to competing products. The industry had known of the perilous status of mercurials prior to cancellation; however, the focus of work was on the concern for mercury entering the environment through manufacture and disposal of waste (29). The undoing of mercury was the result of the inability to contend with predictable misuse, eg, overformulating and use of exterior paint indoors, where indoor air contamination and consequent human intoxication by inhalation could occur.

**Table 7. Metal-Containing Industrial Antimicrobial Agents**

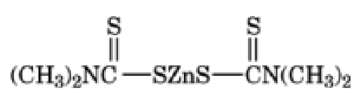
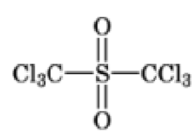
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| 10,10′-oxybisphenoxi-arsine | [58-36-6] | | Vinyzene Durotex | Morton | plastics, textiles |
| | |  | | | |
| tributyltin oxide | [56-35-9] | $(n\text{-}C_2H_9)_3Sn{-}O{-}Sn(n\text{-}C_4H_9)_3$ | Fungitrol | Hüls | antifoulant, paint, plastics |
| tributyltin fluoride | [1983-10-4] | $(n\text{-}C_4H_9)_3SnF$ | Biomet 204 | M&T | antifoulant paint |
| copper 8-quinolinolate | [10380-28-6] | | Cunilate Nytek | Morton | textiles, wood |
| | |  | | | |
| copper naphthenate | [1338-02-9] | | Nuodex | Mooney | textiles, wood |
| chromated copper arsenate | [37337-13-6] | $Cu_3(AsO_4)_2NaCr_2O_7$ | | Kopcote | wood |
| ammoniacal copper arsenate | [32680-29-8] | $CuNH_4AsO_4$ | All Weather Wood | Osmose | wood |
| cuprous oxide | [1317-39-1] | $Cu_2O$ | | American-Chemet SCM-Glidden | antifoulant paint |

The compound 10,10′-oxybisphenoxarsine (OBPA) is a unique organoarsenic antimicrobial. The powerful antimicrobial properties of organoarsenics had long been recognized, and there is plentiful treatment of the synthesis of organoarsenic derivatives in the literature. OBPA is used primarily in the plastics industry, where its high temperature stability and low vapor pressure make it the leading industrial antimicrobial in this market (30).

Use of organotin compounds in marine antifouling applications is governed by the Organotin Antifouling Paint Act of 1988, which limits use to ship hulls greater than 25 m in length and a maximum release rate of

2 $\mu g/cm^2/d$. Organotins are almost always used in combination with some other toxicant (31). Similarly, in water treatment, organotins are used as combination treatment (32).

**Table 8. Organosulfur Industrial Antimicrobial Agents**

| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| | | *Bisthiocyanates* | | | |
| methylenebisthiocyanate (MBT) | [6317-18-6] | $NCSCH_2SCN$ | Cytox 3522 | American Cyanamid | paper mill slimicide |
| | | | Biocide N-948 | Akzo | |
| vinylenebisthiocyanate | [14150-71-1] | NCSCH=CHSCN | Cytox 3711 | American Cyanamid | cooling water slimicide |
| chloroethylenebisthiio-cyanate | [24689-89-2] |  | Cytox 3810 | American Cyanamid | secondary oil recovery |
| | | *Dithiocarbamates* | | | |
| sodium dimethyldithiocar-bamate (Sodam) | [128-04-1] |  | Thiostast Thiostop N | Uniroyal | paint mildewcide, slimicidepaint mildewcide, slimicide |
| disodium ethylenebisdithiocar-bamate (Nabam) | [142-59-6] |  | Dithane D 14 | Rohm and Haas | cooling water slimicide |
| zinc dimethyldithiocar-bamate (Ziram) | [137-30-4] |  | Vancide 51Z | RT Vanderbilt | paper mill slimicide |
| | | *Sulfones* | | | |
| bis(trichloromethyl) sulfone | [3064-70-8] |  | Biocide N-1386 | Akzo | paper mill slimicide, cooling water slimicide, secondary oil recovery |

Copper quinolinolate (oxine copper) is the chelate of divalent copper and 8-hydroxyquinoline and shares most of its market with copper naphthenate, which is a complex copper salt of mixed naphthenic acids. The principal uses are in wood treatments and some military textiles, where the green color is not objectionable. Copper naphthenate has an odor but is cheaper than oxine. Both copper naphthenate and zinc naphthenate have performed well in environment tests, with exposure to soil above-ground, as well as concrete (33).

A variety of copper soaps and complexes, eg, copper oleate [1120-44-1] and copper ethylenediamine tetraacetate [54430-03-1] (EDTA), have also been promoted, but the existence of these minor products is in doubt as a result of the EPA reregistration program mentioned previously. There is an exceptionally rich heritage of organometallic chemistry in the literature which does not have present commercial usefulness but is historically significant (34). Barium metaborate [13701-59-2], $BaO \cdot B_2O_3$, produced by Buckman Labs with the trade name Busan 11-M1, is used as a paint mildewcide. As a result of the concerns surrounding the use of pentachlorophenol, there is a resurgence in interest in copper carbamates. A patent presents a two-step process, involving, first, contacting wood with an aqueous solution of a copper compound, followed by a second immersion, in a carbamate compound, to form an *in situ* treatment (35).

### 6.5. Organosulfur Compounds

These compounds, listed in Table 8, are used in a variety of applications, including cooling water, paint, and metalworking. Methylenebisthiocyanate hydrolyzes rapidly at a pH above 8 to cyanate ion which complexes with ferric iron to poison the cytochrome systems (36).

### 6.6. Heterocyclics

The heterocyclic compounds used as industrial antimicrobial agents are listed in Table 9. Captan and Folpet are agricultural fungicides that have found some industrial uses, primarily in solvent-based paints. Human toxicology concerns have resulted in some diminishing of markets (37). Lack of solubility has limited the formulation flexibility and product is typically available in a malleable concentrate (44–88%) (38). A typical synthesis has been disclosed (39).

**Table 9. Heterocyclic Industrial Antimicrobial Agents**

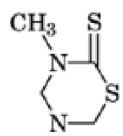
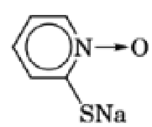
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| | | *Nitrogen–sulfur heterocyclics* | | | |
| tetrahydro-3,5-dimethyl-2*H*-1,3,5-thiadiazine-2-thione (DMTT) | [533-74-4] |  | Metasol D3T<br>Biocide N-521 | Calgon Akzo | paper mill slimicide, paint, cooling water slimicide, adhesives |
| sodium pyridinethione | [3811-73-2] |  | Sodium Omadine | Olin | metalworking fluids, cosmetics |

**Table 9.** ***Continued***

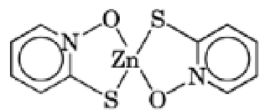
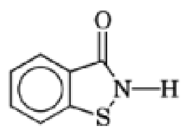
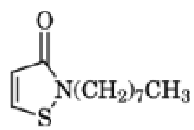
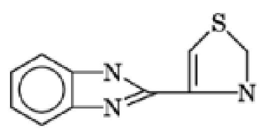
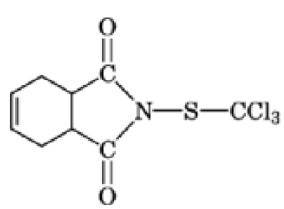
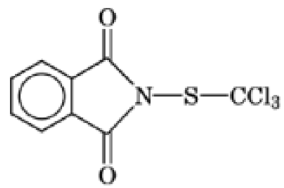
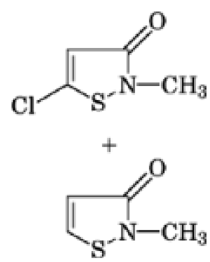
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| zinc pyridinethione | [13463-41-7] |  | Zinc Omadine | Olin | antidandruff agent, cosmetics |
| 1,2-benzisothiazoline-3-one | [2634-33-5] |  | Proxcel CRL | Zeneca | latex paint preservatives, pigment slurries, adhesives, metalworking fluids |
| 2-(*n*-octyl)-4-isothiazolin-3-one | [26530-20-1] |  | Kathon Kathon LP | Rohm and Haas | latex paint mildewcide, leather hides |
| 2-(4-thiazolyl)benzimidazole | [148-79-8] |  | Metasol TK-100 | Merck | latex paint mildewcide |
| *N*-(trichloromethylthio)-4-cyclohexene-1,2-dicarboximide (Captan) | [133-06-2] |  | Vancide 89RE | RT Vanderbilt | paint |

**Table 9.** ***Continued***

| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| *N*-(trichloromethylthio)-phthalimide (Folpet) | [133-07-3] |  | Fungitrol 11 | Hüls | paint |
| 5-chloro-2-methyl-4-isothiazolin-3-one 2-methyl-4-isothiazolin-3-one | [26172-55-4] [2682-20-4] |  | Kathon 886 | Rohm and Haas | paint, metalworking, cooling water, cosmetics |

### 6.7. Other Nitrogen Compounds

The basis of the sophisticated nitrogen compounds listed in Table 10 is the reaction of formaldehyde with amino compounds. A significant amount of literature details investigation of the mechanism of action, particularly whether or not the antimicrobial activity depends on decomposition to formaldehyde (40–42). These compounds tend to have substantial water solubility and are more effective against bacteria than fungi and yeasts. Key markets for these compounds are metalworking fluids, cosmetics, and in-can preservation of paints (see Alkanolamines; Amines, fatty amines).

**Table 10. Industrial Amine, Alkanolamine, and Nitro-Containing Antimicrobial Agents**

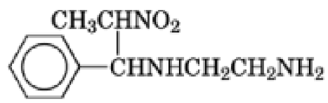
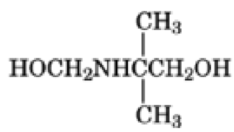
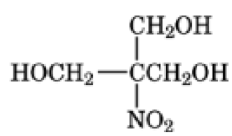
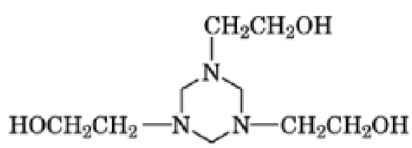
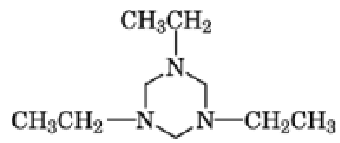
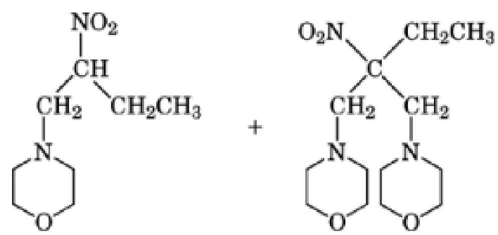
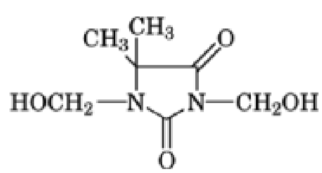
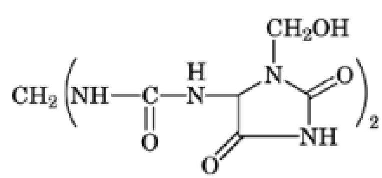
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| | | *Linear* | | | |
| *N*-cocotrimethylenediamine | [61791-63-7] | $RNHCH_2CH_2NH_2$ | | Akzo | secondary oil recovery, cooling water, paper |
| *N*-[α-(1-nitroethyl)benzyl]-ethylenediamine | [14762-38-0] |  | Metasol J-26 | Merck | paper mill slimicide |
| 2-(hydroxymethyl)amino-ethanol | [34375-28-5] | $HOCH_2NHCH_2CH_2OH$ | Troysan 174 Nuosept | Troy Hüls | latex paint, resin emulsion |
| 2-(hydroxymethyl)amino-2-methylpropanol | [52299-20-4] |  | Troysan 192 | Troy | adhesives, tape-joint compound |
| 2-hydroxymethyl-2-nitro-1,3-propanediol | [126-11-4] |  | Tris Nitro | Angus | metalworking, cooling water |
| | | *Cyclic* | | | |
| hexahydro-1,3,5-tris-(2-hydroxyethyl)-*s*-triazine | [4719-04-4] |  | Bioban GK Grotan | Angus Lehn & Fink | metalworking, paint |

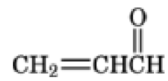
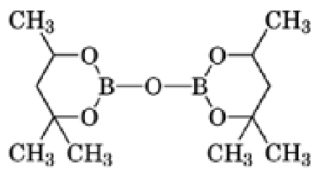
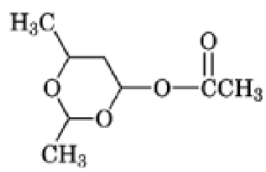
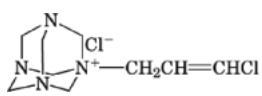
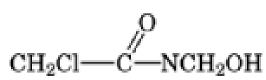
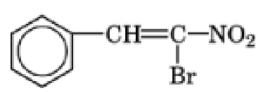
**Table 10.** ***Continued***

| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| hexahydro-1,3,5-triethyl-*s*-triazine | [7779-27-3] |  | Vancide TH | Vanderbilt | paint preservative, rubber latex, adhesive |
| 4-(2-nitrobutyl)morpholine + 4,4′-(2-ethyl-2-nitro-trimethylene)-dimorpholine[a] | [2224-44-4][1854-23-5] |  | Bioban p-1487 | Angus | metalworking fluids |
| | | *Aldehyde-releasing compounds* | | | |
| glutaraldehyde | [111-30-8] | $OCHCH_2CH_2CHO$ | Ucarcide<br>Nuosept 95 | Union Carbide<br>Hüls | cosmetics, metalworking |
| 1,3-dimethylol-5,5-dimethyl-hydantoin | [6440-58-0] |  | Glydant | | cosmetics |
| imidazolidinyl urea | [39236-46-9] |  | Germall 115 | Sutton Labs | cosmetics |

[a]CAS Registry Number for the mixture is [37304-88-4].

Nitromethane is the most reactive nitroalkane that favors strong reaction to the tris adduct (see Nitroalcohols).

**Table 11. Miscellaneous Antimicrobial Agents**

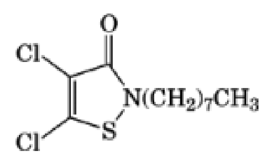
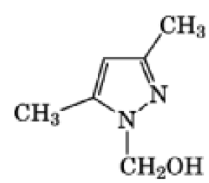
| Chemical name | CAS Registry Number | Structure | Trade name | Producer | Applications |
|---|---|---|---|---|---|
| acrolein | [107-02-8] |  | Aqualin | Baker | oil recovery |
| mixed dioxaborinanes | [14697-50-8] |  | Biobor JF | U.S. Borax | hydrocarbon fuels |
| 2,6-dimethyl, 1,3-dioxanol-4 acetate | [828-00-2] |  | Givguard-DXM | Rhône-Poulenc Rorer | textiles |
| 1-(3-chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride | [4080-31-3] |  | Dowicil 100 | Dow | adhesives, floor waxes, latex emulsions, metalworking fluids, paint |
| 2-chloro-*N*-(hydroxymethyl) acetamide | [6320-16-7] |  | Grotan HD2 | Lehn & Fink | metalworking |
| $\beta$-bromo-$\beta$-nitrostyrene | [7166-19-0] |  | | Rhône-Poulenc Rorer | cooling water, metalworking |

$$CH_3NO_2 + 3\,CH_2{=}O \longrightarrow HOCH_2-\underset{\displaystyle CH_2OH}{\overset{\displaystyle NO_2}{C}}-CH_2OH$$

**Table 12. Antimicrobials of the 1980s**

| Chemical | CAS Registry Number | Name | Registration year |
|---|---|---|---|
| methyl-3,5,7-triaz-1-azoniatricyclodecane chloride | | BusanR 1024 | 1987 |
| 1-(hydroxymethyl)5,5-dimethyl hydantoin | [116-25-6] | Glyco Serve | 1985 |
| 2-bromo-2-nitropropanediol | [52-51-7] | Bronopol | 1984 |
| methanol, [[2-(dihydro-5-methyl-3 (2*H*)-oxazolyl)-1-methylethoxy]ethoxy]methoxyl | | CosanR 145 | 1983 |
| alkyl(61% $C_{12}$, 23% $C_{14}$, 11% $C_{16}$, 5% $C_{18}$) dimethyl benzyl ammonium chloride | [68391-01-5] | | 1982 |

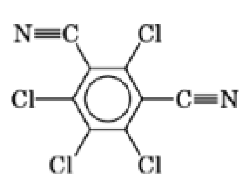
**Table 13. Developmental Industrial Antimicrobials**

| Chemical name | CAS Registry Number | Structure | Producer |
|---|---|---|---|
| 2(*n*-octyl)-4,5-dichloro-isothiozal-3-one[a] | [26530-20-1] |  | Rohm and Haas |
| decylthioethylamine[b] | [29873-30-1] | $CH_3(CH_2)_9SCH_2CH_2NH_2$ | Dow |
| decylthioethylamine-hydrochloride[b] | [36362-09-1] | $CH_3(CH_2)_9SCH_2CH_2NH^+{}_3CL^-$ | Dow |
| *N*-hydroxymethyl-3,5-dimethylpyrazole | [85264-33-1] |  | Buckman |

[a]Trade name, Sea Nine; used as a marine antifoulant.
[b]Trade name, XV-40304-OIL; used for cooling water.

### 6.8. Miscellaneous, New, and Developmental Antimicrobial Agents

Table 11 shows some of the antimicrobials that do not neatly fit into the principal families. Acrolein (qv) is a unique chemical used for secondary oil recovery (43). Biobor has become the antimicrobial addition of choice for aviation fuels (44). Chlorophthalonil (tetrachloroisophthalnitrile [1897-45-6]) is a significant agricultural fungicide, in addition to being one of the most important latex paint film preservatives (producer, ISK).



As noted earlier, the most significant trend in the industry has been the decline in the number of available active ingredients due to EPA regulations. Table 12 shows the new active ingredients, together with the year of their obtaining an EPA registration. Bronopol had actually been used as a preservative for cosmetics prior to its registration (45). The importance of these products is not known.

Table 13 shows some of the developmental products that have EPA applications pending and may be available in the near future. Sea Nine is a variation on the very successful isothiazolone chemistry. It is claimed to be an improvement over metallic actives used for antifouling paint and wood preservation (46, 47). Decylthioethylamine and its water-soluble hydrochloride are claimed to be especially effective at controlling biofilm in cooling water applications (48–50). The hydroxymethylpyrazole shown is also suggested to have properties that are well suited to the protection of aqueous products or emulsions (51, 52).

## BIBLIOGRAPHY

"Industrial Fungicides" under "Fungicides" in *ECT* 1st ed., Vol. 6, pp. 991–995, by R. G. H. Siu, Quartermaster General Laboratories, U.S. Army; in *ECT* 2nd ed., Vol. 10, pp. 228–236, by N. Joe Turner, Boyce Thompson Institute for Plant Research, Inc.; "Industrial Antimicrobial Agents" in *ECT* 3rd ed., Vol. 13, pp. 223–253, by S. I. Trotz and J. J. Pitts, Olin Corp.

### Cited Publications

1. J. G. Holt, ed., *Bergey's Manual of Systematic Bacteriology*, 8th ed., Williams & Wilkins Co., Baltimore, Md., 1984.
2. I. E. Akamo, *Fundamentals of Microbiology*, 4th ed., The Benjamin/Cummings Publishing Co., Inc., 1994.
3. M. J. Pelczar, Jr. and R. R. Reid, *Microbiology*, McGraw-Hill Book Co., Inc., New York, 1972, 72–73, 412, 424–439.
4. L. S. Goodman and H. Gilman, *The Pharmacological Basis of Therapeutics*, 5th ed., Macmillan Publishing Corp., New York, 1975, 946–959, 987–1017, 1090–1129.
5. S. S. Block, ed., *Disinfection, Sterilization, and Preservation*, Lea and Febiger, Philadelphia, Pa., 1991, 20–24.
6. O. Shapiro and L. Magier, *Adhes. Age* **34**, 22–24, (1991).
7. U.S. Environmental Protection Agency, subdivision G, *Product Performance NTIS PB-83-153924,* Washington, D.C., Sept. 1982.
8. H. Rossmoore, *ASTM Standards on Materials and Environmental Microbiology*, American Society for Testing and Materials, Philadelphia, Pa., 1987.
9. A. A. Aspelin and F. S. Bishop, *Chemicals Registered for the First Time as Pesticidal Active Ingredient Under FIFRA*, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C., 1991.
10. *Status of Pesticides in Reregistration and Special Review*, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C., 1992.
11. W. Poppendorf, M. Selim, and N. Lewis, "Exposure While Applying Industrial Antimicrobial Pesticides," *Am. Ind. Hygiene Assoc. J.*, in press (1994).
12. Chemical Manufacturers Association, Biocides Panel, Washington, D.C. personal communication, 1991.
13. E. S. Keische and D. Hunter, *Chem. Week*, 24–25 (July 22, 1992).
14. D. L. Price, A. D. Swant, and D. G. Ahern, *J. Ind. Microbiol.* **8**, 83–90 (1991).
15. U.S. Pat. 5,024,840 (June 18, 1991), L. W. Blakely and co-workers (to Interface, Inc.).
16. Ref. 5, 241–242.
17. J. L. Spier and J. R. Malek, *J. Colloid Interface Sci.* **89**, 68–76 (1982).
18. J. Hanson, *Mod. Paint Coatings*, 50 (1984).
19. Ref. 5, 229–230.
20. Ref. 5, 131–149.
21. J. R. Back, B. R. Friedfeld, and A. A. Boccone, *Biocides—United States*, C. K. Kline, Fairfield, N.J. 1984, p. 29.
22. W. F. McCoy and J. W. Wireman, *J. Ind. Microbiol.* **4**, 403–408 (1989).
23. H. W. Talbot, J. E. Morrow, and R. J. Seidler, *J. Amer. Water Works Ass.* **71**, 349–353 (1979).

24. R. Mullin, *Chem. Week*, 37–40 (May 12, 1993).
25. E. Brantt, *Chem. Eng.* **99**(10) 57, 9 (1992).
26. Ref. 5, p. 142.
27. V. S. Brözel and T. E. Cloete, *J. Ind. Microbiol.* **8**, 273–276 (1991).
28. W. E. Machemer, *Devel. Ind. Microbiol.* **20**, 25–29 (1979).
29. Ref. 5, 334–343.
30. N. M. Rei, T. C. McEntee, and J. F. Brophy, in J. Edenbaum, ed., *Plastics Additives and Modifiers Handbook*, Van Nostrand Reinhold Co., Inc., New York, 1992, 338–355.
31. Ref. 5, 344–357.
32. J. J. Miller, W. E. Brown, and V. J. Krieger, *Devel. Ind. Microbiol.* **22**, 763–770 (1981).
33. R. P. Bratt and co-workers, *Biodeterioration Biodegradation* **29**, 61–73 (1992).
34. M. Dub, *Organo-Metallic Compounds*, Vol. **III**, Springer-Verlag, New York, 1968.
35. U.S. Pat. 4,937,143 (June 26, 1990), M. H. West (to Chapman Chemical Co.).
36. J. W. McCoy, *Microbiology of Cooling Water*, Chemical Publishing Co., New York, 1980, 82–83.
37. *Suspended, Cancelled and Restricted Pesticides*, Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency, Washington, D.C., 1990.
38. J. H. Ayers and D. Lopez, *Chemical Economics Handbook, Fungicides*, SRI International, Palo Alto, Calif., 1984.
39. U.S. Pat. 2,553,770 (May 22, 1951), A. R. Kittleson (to Standard Oil).
40. H. W. Rossmoore and M. Sondossi, *Advances in Applied Microbiology*, Vol. **33**, Academic Press, Inc., San Diego, Calif., 1988, 223–274.
41. M. Sondossi, H. W. Rossmoore, and W. Wireman, *J. Ind. Microbiol.* **1**, 87–103 (1986).
42. C. P. Barnes and R. G. Eagon, *J. Ind. Microbiol.* **1**, 113–118 (1986).
43. Ref. 5, p. 927.
44. C. Genner and E. C. Hill, in A. H. Rose, ed., *Microbial Biodeterioration*, Academic Press, London, 1981, pp. 276, 277.
45. E. L. Richardson, *Cosmet. Toiletries* **96**, 91, 92 (Mar. 1981).
46. J. C. Harrington, *Comparative Effects of Organic Antifoulant Biocides in Marine Paints,* 29th Marine and Offshore Coatings Conference, Charleston, S.C., June 28, 1989.
47. J. Hall, ed., *American Wood Preservers Association Standards* AWPA, Washington, D.C., 1991.
48. U.S. Pat. 4,816,061 (Mar. 28, 1989), R. W. Walter, A. G. Relenyi, and R. L. Johnson (to The Dow Chemical Co.).
49. U.S. Pat. 4,982,004 (Jan. 1, 1992), A. G. Relenyi and C. D. Gartner (to The Dow Chemical Co.).
50. U.S. Pat. 5,025,038 (June 18, 1991), A. G. Relenyi and C. C. Gartner (to The Dow Chemical Co.).
51. U.S. Pat. 4,801,362 (Jan. 31, 1989), J. G. Fenyes (to Buckman Lab International).
52. C. G. Hollis and co-workers, in H. W. Rossmoore, ed., *Biodeterioration and Biodegradation*, Vol. **8**, Elsevier Applied Science, London, 1991.

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