REGULATION OF BACTERICIDES UNDER THE FEDERAL INSECTICIDE, FUNGICIDE AND RODENTICIDE ACT

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On the basis of legislative definition, official regulation, and legal interpretation, all sterilizing, disinfecting, sanitizing, and germicidal chemicals except those sold *solely* for use on or in the living body of man or other animals are *economic poisons* as that term is defined in the Federal Insecticide, Fungicide and Rodenticide Act *(16)* and subject to regulation by the Department of Agriculture *(5)* if shipped in interstate commerce or Federal territories, or received from any foreign country. Economic poisons require registration or preclearance under this law before they are offered for sale. All physical *devices* for controlling bacteria and fungi on or in inanimate materials are also subject to Federal regulation under the provisions of this statute but registration is not required.

A breakdown or classification of antimicrobial economic poisons according to intended end use would include:

1. Surgical and dental instrument sterilizers and disinfectants.
2. Medical and veterinary hospital, clinic and office germicides.
3. Mortician and funeral parlor equipment sterilizers, disinfectants and sanitizers.
4. Barber shop and beauty parlor instruments, equipment and premise sterilizers, disinfectants and sanitizers.
5. Laundry and dry cleaning chemical disinfectants, sanitizers, and bacteriostats.
6. Institution maintenance (janitorial), germicidal and sanitizing chemicals.
7. Dairy, bottling, canning and food processing equipment disinfectants, sanitizers, and sanitizing detergents.
8. Restaurant, tavern, lunch counter, and bar sanitizers and disinfectants for equipment, dishes and glasses.
9. Sewage disposal and chemical toilet germicides.
10. Public drinking water and swimming pool disinfectants and slime control chemicals; and industrial water supply antimicrobial additives.
11. Bacteria and fungus control chemicals employed in secondary oil recovery process waters and brines.
12. Bactericides and bacteriostats sold for use in cutting oils and oil-water emulsion cooling compounds.
13. Household germicides and detergent-sanitizers.
14. Farm building and equipment disinfectants, germicides and sanitizers including products specially used for milking and hatchery equipment.
15. Slime control agents for paper mills.
16. Food, feed and industrial material preservatives where the objective is protection against bacteria and fungi.
17. Air sanitizing chemicals.

Although this classification seems imposing it does not cover a rather large number of smaller group specialty products such as *(a)* disinfectants for reconditioning second-hand brass and reed band instruments (required by some local public health ordinances), *(b)* telephone disinfectants, and *(c)* detergent-sanitizers for contact lenses and the like, all of which are likewise subject to the law. Devices subject to the provisions of the law include:

1. Sanitizing ultra-violet lamp assemblies.
2. Heat sterilizers.
3. Pasteurizers.
4. Ozone generators sold under labeling bearing antimicrobial claims.
5. Bacteriological filters.

Registrations on economic poisons are issued without pretesting based on the Department's best judgment of the representations and supporting information submitted by the manufacturer or applicant. All proposed labels are reviewed by Department specialists to determine *(a)* the suitability of the proposed name, *(b)* if the net content and ingredient statements are in agreement with the forms permitted in the law, *(c)* the presence of the name and address of the manufacturer or distributor, *(d)* if the label bears caution and warning statements adequate for the protection of the general public, and *(e)* adequacy of the directions for use given.

In the case of the net content statement, the ingredient statement, the need for precautionary labeling, and the manufacturer's or distributor's name and address, the requirements are set *within* the law itself. The net contents must be given in the case of liquids as fluid ounces, pints, quarts or gallons, whichever is the largest single unit present, and in the case of powders, solids and gases (including pressurized containers) as avoirdupois ounces or pounds, whichever is the largest single unit present. Only two forms of ingredient statements can be accepted. In the first form the correct name and percentage by weight of each active ingredient and the total percentage by weight of the inert ingredients must be given. In the second form the correct names of all active and inert ingredients respectively must be given in the descending order of the percentages of each present in each classification and the total percentage by weight of the inert ingredients must be shown. The law defines as active ingredients those which have activity *per se* in the uses recommended and are present in the formula in sufficient concentrations to contribute to the over-all activity. Inert ingredients are defined as those which do not have activity *per se* in the uses recommended, are antagonistic

to the principal active ingredients or those which although possessing activity *per se* are not present in sufficient amounts to contribute to the over-all activity of the formula.

Names which clearly imply that a product is something different than that which it is or possesses properties other than those which it actually possesses are considered unsuitable and are not acceptable. For example, it is held to be improper to identify a product as a pine or pine oil disinfectant if it does not comply with the accepted commercial standards for pine oil disinfectants *(15)*. Also, it is held to be improper to represent a product as a sterilizer when it will not sterilize when used as directed.

Precautionary labeling requirements must be patterned to cover the dangers inherent in handling the product as sold, as well as those associated with use as directed. Four general categories of toxicity are recognized. The first is the highly toxic class as defined in the regulations as those products which produce death in half or more than half the animals of any species at a dosage of 50 milligrams at a single dose or less per kilogram of body weight when administered orally; those which produce death in half or more than half of the animals of any species at a dosage of 200 parts or less by volume of the gas or vapor per million parts by volume of air in continuous inhalation for one hour or less; and those which produce death in half or more than half of rabbits tested at a dosage of 200 milligrams or less per kilogram of body weight when administered by continuous contact with the bare skin for 24 hours or less. The second is the class immediately below the highly toxic and in general includes formulations having toxicities down to one-tenth those of the highly toxic class. The third group embraces products having hazards down to about one-tenth of those in class two. The fourth class is comparatively free from danger.

Highly toxic products are required to be labeled with the skull and crossbones, the word "Poison" in red on a contrasting background and an antidote statement including the words "Call a physician immediately." Labels for products in the second category require warning statements practically equivalent to those specified for highly toxic products except that they need not bear the skull and crossbones, the word "Poison" or an antidote statement. As a substitute for the word "Poison" a statement such as "Warning, may be fatal if swallowed, inhaled, or absorbed through the skin" is required. Labels for products in the third category are required to carry the word "Caution" and statements outlining the means of avoiding the principal hazards of use and handling. Category four products usually do not need warning, caution or antidote statements although unqualified claims for safety can seldom be justified.

Precautionary labeling requirements must take into account such factors as fire hazards, potential injury to fish, wildlife, beneficial insects, food contamination, injury to crops and the possibility of accidental injury to small children and other individuals who cannot read because of blindness or lack of education.

The Department holds that directions which will give the results claimed when applied in all the applications recommended are necessary to meet the term "adequate" stipulated in the law. Determinations as to the adequacy of the directions with different chemicals for all of the antimicrobial applications listed above provide real challenges for the Department specialists.

Where standards have been set in U. S. Public Health Service recommended ordinances and codes as in the case of the "Milk Ordinance and Code, 1953 Recommendations of the Public Health Service" *(10)* and the "Ordinance and Code Regulating Eating and Drinking Establishments" *(11)* it is not too difficult to set up minimum requirements for registration on which an effective enforcement program can be developed.

Where no uniform Federal recommendations as to public health ordinances and codes exist and where no official medical, veterinary medical, dental or other professional standards have been established and where a wide variety of municipal, county and state codes do exist the Department sets the minimum requirements for registration based both on a consensus of existing codes and its own best estimation as to the level which adequate public protection requires and where there is reason to believe an effective enforcement program is possible. Typical examples of this situation are "Barber shop and beauty parlor disinfectants and devices" *(6, 7, 8, 9)*, and "Swimming and Wading Pool Germicides and Devices."

With those applications and products where neither local or Federal public health ordinances or recommendations exist the minimum requirements for registration are set according to evaluations of the available scientific literature, information furnished by applicants and/or tests in the Department laboratories.

Acceptance for registration should not be interpreted as a recommendation by the Department. The manufacturer is responsible for all claims which appear on either a registered or unregistered label. Registration is simply a means through which products are brought to the attention of the Department, affording an opportunity to obtain precautionary

labeling which may be necessary to protect the public and to correct obvious defects insofar as the various other requirements of the law are concerned.

The Department operates an aggressive enforcement as well as an effective registration program. It maintains a staff of field investigators who collect samples of registered and unregistered products from shipments made in interstate commerce. The labeling of all samples collected is checked against the registration files, the samples are then analyzed chemically, tested bacteriologically to determine the validity of the claims and directions for use and checked by the pharmacologist if necessary to determine whether or not the precautionary labeling meets with legal requirements.

The law provides authority for a number of enforcement actions. Interstate shipments of economic poisons made without registration or which are deemed to be adulterated or misbranded may be seized by the appropriate United States Attorney upon recommendation by the Department. This is a civil action against the merchandise. Criminal proceedings may be initiated against the manufacturer after notice of violation has been sent directly by the Department to the shipper of any economic poison which *(a)* has not been registered, *(b)* is shipped under labeling bearing claims and representations differing in substance from those made in connection with its registration, or *(c)* is misbranded and/or adulterated affording him an opportunity to make such explanation of the violation in writing or orally as may be possible. If a reasonable explanation cannot be made the case may be referred to the proper United States Attorney for prosecution. There are also certain provisions for the cancellation of registrations which can be employed as enforcement aids. It should be made a matter of record, however, that many technical and minor violations are corrected voluntarily each year by manufacturers simply through informal correspondence calling deficiencies to their attention.

The effectiveness of the Department's program insofar as determinations as to the validity of claims and the adequacy of application directions for antimicrobial chemicals are concerned depends largely upon the establishment of standardized laboratory testing methods which yield results that can be accurately interpreted in terms of actual use concentrations and modes of application.

Laboratory testing methods are continually being evaluated as to their suitability for referee use under the auspices of the Association of Official Agricultural Chemists. As rapidly as proposed methods are found to be accurate and precise enough for acceptance they are published and made available by that organization.

In the case of disinfectants, germicides, sanitizers and detergent-sanitizers recommended for use on dairy utensils, food processing equipment, cooking utensils, and dishes and glasses in restaurants, taverns and bars there are two official A.O.A.C. methods which have been found to have special merit. These can be identified as the "Available Chlorine Germicidal Equivalent Concentration Test — Official" *(2)* and the "Germicidal and Detergent Sanitizers Test — Official *(13)*. The former provides an accurate index to the public health value of organic chlorine bearing chemicals and halophor formulations as germicidal rinses for previously cleaned dairy and food processing equipment as well as dishes and glasses in restaurants. The latter which may be more commonly recognized as the Chambers Test *(3)* or the Weber and Black Method *(21)* provides satisfactory data insofar as water-hardness tolerances of quaternary ammonium formulations recommended for dairy, food plant and restaurant use are concerned, and the minimum concentrations of germicidal formulations which can be permitted in use at any time in washing or rinsing dairy utensils, food processing equipment or dishes and glasses in restaurants, taverns and bars. Both methods take into account the necessity for quick bactericidal action with products recommended for these applications. It has been determined *(12)* that the 30 second end point in the "Germicidal and Detergent Sanitizers Test — Official" with alkaline sodium hypochlorite is at the 50 p.p.m. available chlorine concentration and that the one test culture increment-one minute end point in the "Available Chlorine Germicidal Equivalent Concentration Test — Official" is 50 p.p.m. of available chlorine as alkaline sodium hypochlorite. Thus, results obtained by the two methods are directly comparable. Since neither method alone is entirely satisfactory for all of the evaluations which need to be made on products in this class this is an essential and fortunate circumstance.

While public health officials are concerned with the concentration and activity of the product in use at any time the Department is primarily concerned with the activity and concentration of the solution which must be recommended at the beginning of the sanitizing operation to assure the minimum activity required by the public health inspector at any time. With alkaline hypochlorites the pattern of public health acceptance is firmly established. Solutions providing 100 p.p.m. of available chlorine are required at the beginning of the sanitizing operation where chemical facilities are available to test the concentration of the solution in use so that it will not fall below 50 p.p.m. of available chlorine at any time. Where such testing facilities are not available, the con-

centration of the starting solution must be high enough to provide 200 p.p.m. of available chlorine. This accepted use pattern is employed as a guide for the interpretation of data obtained with the two methods referred to above in terms of the acceptable concentrations of starting solutions with the various products submitted for registration and/or sampled by Department investigators. The "Available Chlorine Germicidal Equivalent Concentration Test — Official" is especially adapted to determinations as to the minimum concentrations necessary to recommend for starting solutions with formulas prepared from organic chlorine bearing chemicals, and mixed halogens, iodophors and peroxides. It is a relatively simple and uncomplicated procedure which provides with a remarkable degree of precision a direct measure on the concentration of such formulas that possess equivalent speed and capacity of kill to solutions of sodium hypochlorite at p.H 8.5 providing 50, 100 and 200 p.p.m. of available chlorine. Its effectiveness in the Department's registration and enforcement program with products recommended for those applications where these concentrations of sodium hypochlorite have been accepted as public health standards clearly suggests that modifications might be developed for use in connection with the regulation of drinking water and swimming pool water disinfectants where minimum available chlorine concentrations as hypochlorite have widespread public health acceptance.

The "Germicidal and Detergent Sanitizers Test — Official" provides a reasonably accurate index to the hard water tolerances of quaternary ammonium compound formulations. Claims for effectiveness in hard water are not accepted for registration unless the applicant submits supporting satisfactory experimental evidence using this procedure. Hard water label claims on official regulatory samples are checked by this method. This test has also been applied successfully in investigations on the effectiveness of various sequestrants on the hard water tolerances of formulas and in studies on the relation of molecular structure in quaternaries to hard water tolerances. It appears to have a ± 10% coefficient of variation in such applications. When applied to determine the minimum concentration of a given product which can be permitted in use at any time distilled water solutions are usually employed. Distilled water solutions of the more active quaternaries may give the required 30 second, 99.999% reduction end point in this method at concentrations as low as 15 p.p.m. *(17)*. In such a situation consideration could be given to recommending a starting concentration of 60 p.p.m. based on the fact that no chemical test for determining the residual concentration of active quaternary in use has received public health approval and acceptance of the concentration multiples of 2 and 4 required with hypochlorites. This is considerably below the commonly recommended 200 p.p.m. concentration with this type of chemical. While it might be considered acceptable by the Department a recommendation at this level is seldom encountered since it would usually limit any proposed hard water tolerance claim to a level too low for widespread geographic acceptance. Many manufacturers and some public health officials are prone to recommend or specify concentrations of chemicals acceptable as germicidal rinses of previously cleaned hard nonporous surfaces for disinfecting porous table tops, floors, walls and other surfaces where the efficiency of the precleaning operation falls far below that attainable with dishes and glasses in restaurants, stainless steel, glass or monel metal found in dairy and food processing equipment. The Department holds that higher concentrations must be provided with all types of chemical formulations for such applications. The concentrations required to disinfect such surfaces are determined by the A.O.A.C. Use-Dilution Test — Official *(1)*.

In the administration of the law the terms "sanitize" and "disinfect" are not considered to be synonymous. In most applications to disinfect would be to sanitize. However, the word "sanitize" carries with it the connotation of cleanliness and it is difficult to envisage the designation of a disinfected fecally contaminated board as sanitized unless the process involved a cleaning operation. On the other hand, the Department is willing to concede that in day to day maintenance operations where no specific disease organisms are known or suspected of being present, applications of germicidal chemicals at concentrations and in modes of application that could not always be relied upon to provide disinfection in the accepted meaning of the term may furnish the practical result desired. It is not uncommon therefore to accept products as sanitizers under directions for use which would not be acceptable for a disinfecting claim.

Combination detergent-sanitizers and germicidal-detergents are accepted for registration for a rather wide variety of applications. Such designations clearly imply that these products possess practical value as cleaners as well as in sanitizing and/or disinfecting. In the case of a detergent-sanitizer designation *(18)* it is held that the manufacturer is representing his product to the public as something more than an ordinary cleaner and that it must possess activity in the uses recommended in reducing bacterial populations significantly greater than that associated with a cleaning operation using either white floating soap or tetrasodium pyrophosphate. A variety of simulated use tests have been employed

with success to support enforcement activities on this point. In the case of a germicidal-detergent it is held that if a product is so designated the label must bear adequate directions for applying the product in a manner that will both clean and disinfect. If evidence is available to show that both results can be obtained in one operation directions for application in this manner may be accepted as adequate. If the evidence indicates that an initial cleaning operation followed by a rinse with a fresh solution is necessary to assure disinfection then the directions given on the label must specify application in this manner.

At this time the impact of the many new laws enacted by State and Federal legislatures with the stipulated objective of protecting the public from the danger of chemicals on the distribution and use of germicides cannot be accurately measured in its entirety but it would seem that it will not be as great as some individuals have predicted. In some instances exemptions have been made for products subject to the Federal Insecticide, Fungicide and Rodenticide Act. In others some overlapping authorities have been created. Whenever and wherever the latter situation develops the Department works with the enforcement agency involved to clarify the situation as rapidly as possible. No major changes in registration requirements are anticipated although it is only reasonable to suppose that certain minor adjustments in labeling requirements may be necessary with specific chemicals in some recommended applications.

From a sales promotion standpoint an almost unbelievable circumstance exists with germicidal chemicals. At a time of apparent widespread public alarm over the potential dangers of exposure to traces of chemicals found in the atmosphere, drinking water and food as well as through skin contact with such inanimate materials as clothing and surfaces like the interior walls of dwellings, the distributors of this class of compounds have elected to initiate an agressive program extolling the potential benefits of active chemical residues in environmental sanitation programs. This situation has created some very difficult regulatory problems. Reliable information as to the levels of antimicrobial activity which can reasonably be expected from residues of the various germicidal chemicals on paper and fabrics, in paints, floor waxes and similar commodities is meager or nonexistent. No extensive public health studies have been conducted which either establish or disprove the existence of practical sanitation values in the various applications proposed. Each possible benefit must always be weighed against the potential hazard to the consumer and data on the effect of exposure of the human organism to an environment saturated with the specific chemicals known to possess residual antimicrobial activities does not exist. In spite of all this the Department has developed a reasonably effective regulatory program for products to which germicidal chemicals have been added. This has been outlined in two recent publications *(19, 20)*. It is based on the simple premise that a manufacturer is entitled to make such claims for his product as there is reason to suspect may be true providing safety in the recommended applications can be established. It should be emphasized, however, that the Department's responsibility to the consuming public makes it impossible to countenance recommendations for applications in which there is no apparent reason to expect a useful function.

Under the terms of the Miller Bill, Public Law 518, an Amendment to the Federal Food, Drug and Cosmetic Act *(14)*, petitions for residue tolerances or exemptions for bactericides and bacteriostats recommended for use in the production, storage, and transportation of raw agricultural commodities cannot be considered by the Food and Drug Administration until, *(a)* an application for registration under the Federal Insecticide, Fungicide and Rodenticide Act has been filed with the Department of Agriculture, *(b)* a certificate of usefulness issued, and *(c)* an opinion rendered relative to the correctness of the tolerance requested. In the case of the products under consideration here the number involved is not large. However, large numbers of germicidal and sanitizing chemicals registered under the Federal Insecticide, Fungicide and Rodenticide Act are recommended for use in connection with the processing of food. Based on policy statements presently available it would appear that their status under the Food Additives Amendment of the Federal Food, Drug and Cosmetic Act *(4)* will depend largely upon the modes of application specified on the label.

This brief outline covering the scope of the Department's legal responsibilities, the activities of the supporting functions required for enforcing the law, and the general requirements for sterilizers, germicides, bactericides, disinfectants and sanitizers includes only a few specific illustrations. These have been selected from the problems encountered with products sold to the milk and food industries. The sanitation and/or public health requirements in these industries have been much more firmly established than is the case with most of the other consumers of bactericidal chemicals. This materially simplifies the Departments activities in this area. There appears to be a growing interest in the problems of environmental sanitation in other areas but the need for critical studies in these other areas exceeds the interest shown by bacteriologists and public health officials. Until such a time as firm and

uniform agreements can be arrived at by public health officials for many of these other applications the registration requirements and enforcement activities in the Department will in all probability be pitched at a somewhat lower level with products sold for these uses than is the case with products sold for application by milk and food processing companies.

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