Medecide Formulation components: US Regulatory Review

The active ingredients in Medetech's Medecide formulation are members of a large group of biodegradable compounds known Haloimidazolidinones or more commonly Halohydantoins. Chemicals in this class have been relied upon for many US consumer product formulations for more than 50 years. As the uses and types of compounds in this group expanded over the years the US Environmental Protection Agency (US EPA) has conducted comprehensive reviews of their safety and fate in the environment about every ten years, in a process termed "Re-registration" of existing approved registered products. The last re-registration of this group was completed by the Antimicrobial Division of the agency in 2013 (Case # 3055), and is available on the USEPA website at EPA-HQ-OPP-2013-0220-0008.

The re-registration process covers all available data on:

- The analytical chemistry of halohydantoins
- The structure-activity relationships that are involved in mechanisms of action and safety, the animal and ecological system toxicology
- Data from rigorous investigation of any adverse or allergic effects of members of the chemical group that have been reported from consumer or industrial uses since the last review

The US EPA review was rigorous and is thoroughly covered in the agency's 95 page report. It includes primary data on the following topics:

1. The chemical identification and properties of all the halohydantoins
2. The EPA-approved summary of registered uses of the compounds as disinfectants and sanitizers
3. Approved use patterns on registered labels
4. Regulatory history of all the compounds
5. Complete human health risk assessment
6. All records of any incidents of reported side effects to date
7. An assessement of consumer residential and industrial exposures to halohydantoins, including possible aggregate and cumulative exposure effects
8. Environmental fate of all compounds in this class of chemicals

9. Ecological exposures including wildlife and aquatic organisms including freshwater fish
10. Any interactions of these chemicals that could lead to endocrine disruption in the environment
11. A comprehensive compilation of scientific literature references on the halohydantoins

In addition there are provided five Appendices (A through E) that include primary data on the compounds under a range of the headings (chemical toxicology, environmental fate, ecotoxicology, down-the -drain analysis of residues). The report includes 15 data tables and 7 graphic figures.

Uses of chemicals the EPA considered in this series covered applications in food processing, food and beverage containers, water treatment, hard surfaces (floors, tables, countertops, sinks, bathrooms, etc.), pools and spas, and on eggs, fruit and vegetables.

There is an estimated annual consumption of halohydantoins in the US of >16 million kgs/year.

Conclusion: As a result of this year-long comprehensive review no compounds in this series were de-listed from the registry. No uses were curtailed in any way. This decision was an important endorsement of:

1. **The safety of this entire class of compounds**
2. **The continued availability of the imidazolidinones/hydantoins as components of a wide range of products entering the stream of commerce in the USA, and destined for consumer and industrial uses.**

There are components of Medecide that make up the unique formulations covered by US patents granted to date (*10,028,482* (2018) *10,131,73*1 (2019),*10,512,705* (2019)) that are not biocidal and not included in the Re-registration review (stabilizers, surface binding agents, dispersants). These are commonplace constituents of consumer products, pose no hazards to either users or waste streams, and include items that are Generally Regarded as Safe (GRAS) by the US Food and Drug Adminstration as food additives.

The wide range of options of active compounds available for integration into Medecide products is illustrated by the list below:

Medecide Active constituent options covered by the US patent:

The subject invention more specifically reveals a water-based disinfecting and deodorizing fluid which is comprised of (a) at least one water soluble/dispersible N-halamine including but not limited to N-chloro-N-sodiomethylbenzenesulfonamidate trihydrate, N,N-dichloro-4-methylbenzenesulfonamide, N-bromo-N-sodio-4-nitrobenzenesulfonamidate, N,N-dichlorobenzenesulfonamide, N-chloro-N-sodiobenzenesulfonamidate, mono-chlorosulfamate, dichlorosulfamate, N-chloroimidodisulfonates, sodium N-chloro-N-arylsulfamates, 2,4,6,8-tetrachloro-2,4,6,8-tetrazobicyclooctane-3,7-dione, sodium trichloroimidometaphosphamate, N-halosulfinylamines, N-halo-N-sodioamidates, chloroisocyanurates, N-halocarbamidates, N-halosulfonamidates, N-chloro-

imidodisulfonate, N,N-dichloromethylamine, 2-chloro-1,3,5-triazine-2,4,6-triamine, 2,4-dichloro-1,3,5-triazine-2,4,6-triamine, 2,4,6-trichloro-1,3,5-triazine-2,4,6-triamine, 1-chloro-5,5-dimethylhydantoin, 1-bromo-5,5-dimethylhydantoin, 1,3-dibromo-5,5-dimethylhydantoin 1-chloro-3-bromo-5,5-dimethylhydantoin, 1,3-dichloro-5,5-dimethylhydantoin, 1-chloro-4,4,5,5-tetramethylimidazolidin-2-one, 1,3-dichloro-4,4,5,5-tetramethylimidazolidin-2-one, 1-chloro-2,2,5,5-tetramethylimidazolidin-4-one, 1,3-dichloro-2,2,5,5-tetramethylimidazolidin-4-one, 1,3-dichloro-s-triazine-2,4,6-trione, trichloroisocyanuric acid, potassium dichloroisocyanurate, sodium dichloroisocyanurate, potassium dibromoisocyanurate, sodium dibromoisocyanurate, mono to hexachloromelamine, mono to hexabromomelamine, 3-chloro-4,4-dimethyl-2-oxazolidinone, N-chlorosuccinimide, 1-chloropyrrolidine-2,5-dione, 1,3-dichlorotetrahydroquinazoline-2,4-dione, 1,4-dichloro-2,2,5,5-tetrasubstituted-piperazine-3,6-diones, N-chloro-2,2,6,6-tetramethyl-4-piperidinol, N-chloro-2,2,6,6-tetramethylpiperidine, N-chloro-4-amino-2,2,6,6-tetramethylpiperidine, polymer-bound N-chloro-N-sodiobenzenesulfonamidates, chlorinated polyacrylamide, brominated polyacrylamide, chlorinated poly(methacrylamide), brominated poly(methacrylamide), poly(N-chloro-2,2,6,6-tetramethyl-4-piperidinyl acrylate), poly(N-chloro-hydantoin-methyl-p-styrene) emulsion, 1-chloro-3-bromoalkyltrimethylammonium-4,4,5,5-tetramethyl imidazolidin-2-one, 1-bromo-3-bromoalkyltrimethylammonium-4,4,5,5-tetramethyl imidazolidin-2-one, 1-chloro-3-bromoalkyltrimethylammonium-2,2,5,5-tetramethyl imidazolidin-4-one, 1-bromo-3-bromoalkyltrimethylammonium-2,2,5,5-tetramethyl imidazolidin-4-one, 2-chloro-4-bromoalkyltrimethylammonium-1,3,5-triazine-2,4,6-triamine, 2-bromo-4-bromoalkyltrimethylammonium-1,3,5-triazine-2,4,6-triamine, 1-chloro-3-bromoalkyltrimethylammonium-5,5-dimethylhydantoin, and 1-bromo-3-bromoalkyltrimethylammonium-5,5-dimethylhydantoin; and

(b) at least one water soluble halogen stabilizing compound selected from the group consisting of hydroquinone, (2,2,6,6-tetramethylpiperidin-1-yl)oxy, 2,2,6,6-tetramethyl-piperidine-1,4-diol, 2,2,6,6-tetramethyl-4-piperidinol, 4-amino-2,2,6,6-tetramethylpiperidine, 2,2,6,6-tetramethylpiperidine, 2,2,6,6-Tetramethyl-4-piperidyl methacrylate, 2,2,6,6-tetramethyl-4-piperidone, (2,2,6,6-tetramethylpiperidin-4-yl) benzoate, 1,1'-ethylenebis(3,3,5,5-tetramethylpiperazinone), 4-acetamido-2,2,6,6-tetramethylpiperidine, bis(2,2,6,6-tetramethyl-4-piperidyl) succinate, bis(2,2,6,6-tetramethylpiperidin-4-yl) butanedioate, bis(2,2,6,6-tetramethylpiperidin-4-yl)hexane-1,6-diamine and other water soluble derivatives of 2,2,6,6-tetramethyl piperidine.