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Sincerely,



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MEMO TECHNICAL REPORT**

Report No: 1999-I0000-47945
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Date: November 29, 1999
Title: Interim Exposure Assessment for Silicone Antifoams in Food Processing and Over-the-Counter (OTC) Antigas (AG) Products

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Title: Interim Exposure Assessment for Silicone Antifoams in Food Processing and Over-the-Counter (OTC) Antigas (AG) Products

Author: Michael E. Thelen

Date: November 29, 1999

Department: Health & Environmental Sciences, Regulatory

ABSTRACT

This interim exposure assessment was conducted to estimate the potential exposure to octamethylcyclotetrasiloxane (D_4), decamethylcyclopentasiloxane (D_5) and dodecamethylcyclohexasiloxane (D_6) from the use of silicone antifoams in food processing and antigas products (used for treating indigestion and upset stomach) in the U.S. D_4 , D_5 and D_6 are present as residual materials in silicone antifoams as they are used as raw materials to make the silicone polymer contained in silicone antifoams.

Based on an understanding of the route of exposure, the amount, the duration and the frequency of exposure, an estimate of the average daily dose (ADD) for D_4 , D_5 and D_6 was calculated. Oral ingestion is the primary route of exposure for D_4 , D_5 and D_6 from consuming food that was processed with silicone antifoams or from using antigas products that contain silicone antifoams. The ADD's for D_4 , D_5 and D_6 from the consumption of food that has been processed with silicone antifoam do not exceed .002 mg/kg/day, .001 mg/kg/day and .0004 mg/kg/day for infants respectively and .0007 mg/kg/day, .0005 mg/kg/day and .0002 mg/kg/day for adults. The ADD's for D_4 , D_5 and D_6 from using antigas products that contain silicone antifoams were calculated using both market research data to determine the frequency of use for adults and the maximum daily use as specified on the product label. The ADD's for D_4 , D_5 and D_6 for adults do not exceed 1.72×10^{-5} mg/kg/day, 2.02×10^{-5} mg/kg/day and 1.21×10^{-5} mg/kg/day respectively based on frequency of use data from market research studies and 3.70×10^{-4} mg/kg/day, 4.33×10^{-4} mg/kg/day and 3.3×10^{-4} mg/kg/day assuming the maximum daily use as recommended on the product label. The ADD's for D_4 , D_5 and D_6 for infants and children were calculated on a maximum daily use basis due to the lack of market research data on frequency of use. The estimated ADD's for D_4 , D_5 and D_6 for infants do not exceed .12 mg/kg/day, .08 mg/kg/day and .028 mg/kg/day, respectively, and .147 mg/kg/day, .1 mg/kg/day and .034 mg/kg/day for children. The ADD's calculated in this study use default assumptions that provide the reader with a conservative assessment of the exposure to D_4 , D_5 and D_6 through the use of silicone antifoams in food processing and the consumption of antigas products.

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List of Acronyms

AA	antacid
ADD	average daily dose
AF	antiflatulent
AG	antigas
cs	centistokes
D4	octamethylcyclotetrasiloxane
D5	decamethylcyclopentasiloxane
D6	dodecamethylcyclohexasiloxane
DCC	Dow Corning Corporation
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
GMP	good manufacturing practice
LEV	local exhaust ventilation
mg/kg/day	milligrams per kilogram per day
ml	milliliters
MM	million
MRI	Mediamark Research Incorporated
OTC	over-the-counter
PDMS	polydimethylsiloxane
ppm	parts per million
RMDDU	recommended maximum dose during use
SMC	simethicone
tsp	teaspoon

Introduction

The purpose of this report is to summarize and quantify the exposure to octamethylcyclotetrasiloxane (D₄), decamethylcyclopentasiloxane (D₅) and dodecamethylcyclohexasiloxane (D₆) through the use of silicone antifoam products in food processing and Over-the-Counter (OTC) Antigas (AG) Products. Silicone antifoam products are used to control the foaming that occurs in various stages of food processing applications and act as a defoaming agent in the digestive system. The study materials, D₄, D₅ and D₆ are found in trace amounts in polydimethylsiloxane (PDMS), a polymer produced primarily from the above mentioned siloxanes, which is a major component in the manufacturing of silicone antifoams.

Background

- Silicone Antifoams in Food Processing

Silicone antifoams are used in a wide range of processing applications such as food, chemical, petrochemical, waste treatment, adhesives/coatings, metal working, paper/printing and textiles.¹ Antifoams in food processing are treated as a separate application primarily because the *Food and Drug Administration (FDA)* has defined specific requirements for materials that are considered food additives. Silicone antifoams are used in the processing of a wide range of food products, including soft drinks, potato chips, and canned fruit and are added directly to food as process aids, as such they are considered to be *secondary direct food additives*². Appendix A contains a description of what constitutes a food additive according to FDA regulations.

Figure 1 provides a schematic of the applicable regulations for those materials that may be considered food additives. Silicone Antifoams must comply with 21 *Code of Federal Regulations (CFR)* 173.340, the key regulation for antifoams added directly to food. Silicone antifoams are defined as "Dimethylpolysiloxane (substantially free from hydrolyzable chloride and alkoxy groups; no more than 18 percent loss in weight after heating 4 hours at 200°C; viscosity 300 to 1,050 centistokes at 25°C; refractive index 1.400-1.404 at 25°C)". Silicone antifoams are subject to the following limitations "10 parts per million in food or at such level in a concentrated food

¹ Dow Corning® Product Literature, "Dow Corning® Silicone Foam Control Agents User Selection Guide", Form No. 24-372B-93

² Dow Corning® Product Literature, "Silicone Antifoams and Release Agents for the Food Processing Industry", Form No. 24-870C-94

that when prepared as directed on the labels, the food in its ready-for-consumption state will have not more than 10 parts per million except as follows: Zero in milk; 110 parts per million in dry gelatin dessert mixer labeled for use whereby no more than 16 parts per million is present in the ready-to-serve dessert; 250 parts per million in salt labeled for cooking purposes, whereby no more than 10 parts per million is present in the cooked food³.

- Silicone Antifoams in Over-the-Counter Antigas Products

Silicone antifoams used in the formulation of Over-the-Counter (OTC) Antigas products are classified as simethicone (SMC), the active ingredient used in the formulation of antigas (AG) or antifatulent (AF) products. SMC acts as a defoaming agent by reducing the surface tension of small gas bubbles present in the digestive system permitting the formation of larger gas bubbles, which are found to be more easily eliminated by belching or flatus. The FDA considers SMC safe and effective as an AF agent, but limits the maximum daily dose to 500 mgs.³ AFs are sold as "stand-alone" products and/or in combination with certain antacid (AA) products.

³ Code of Federal Regulations (CFR), Part 332 - "Antiflatulent Products for Over-the-Counter Human Use," Section 332.1, Scope.

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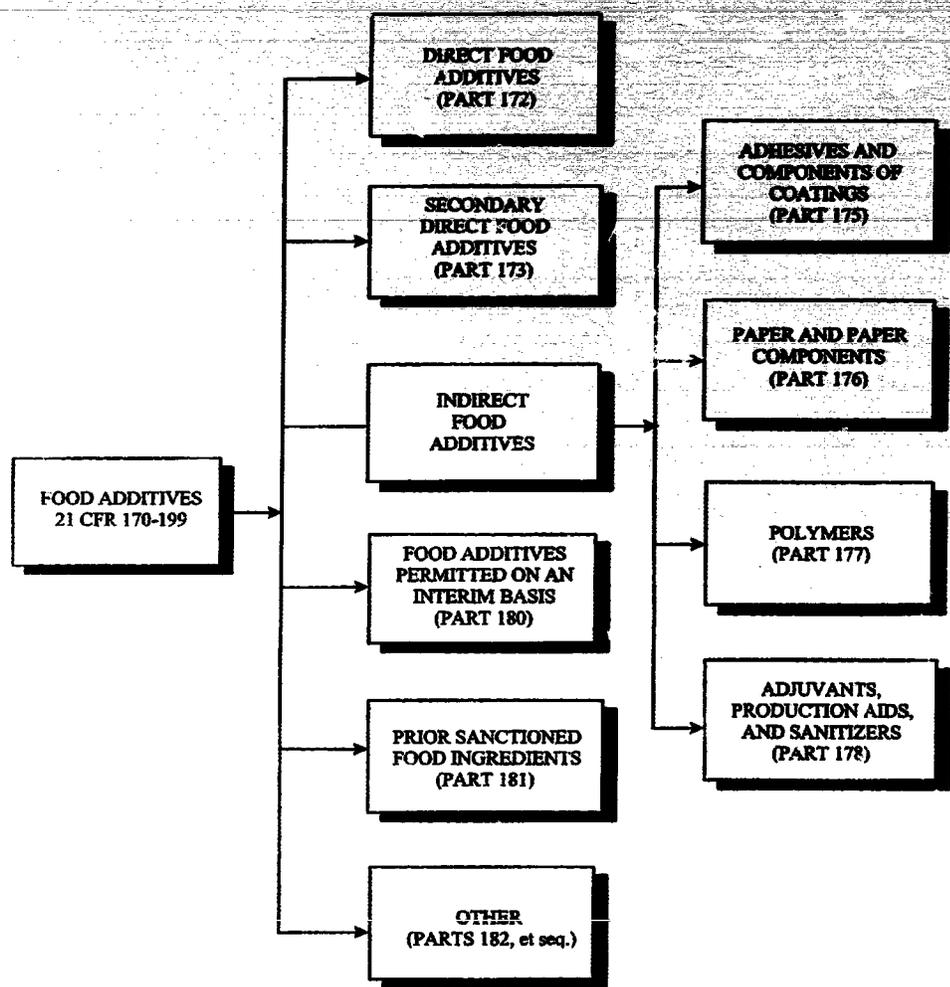


FIGURE 1. SCHEMATIC OF FDA REGULATIONS FOR FOOD

Description of Silicone Antifoams

Antifoams and/or defoamers are materials that either prevent the formation of foam or result in its elimination. In general there are three types of antifoams; nonpolar oils such as polydimethylsiloxane (PDMS) fluid or mineral oil, hydrophobic silica or hydrophobic polymers, and mixtures of nonpolar oils and hydrophobic silica.⁴

In most applications, silicone antifoams are mixture of PDMS and silica. Cyclic siloxane fluids (which include D₄, D₅, and D₆) are polymerized to form PDMS in a high-temperature/low-pressure process. The PDMS, which contains trace quantities of D₄, D₅, and D₆, is then compounded with a silica filler. PDMS has the general chemical formula:



For PDMS used in silicone antifoams in food applications n is approximately 100 to 200 and approximately 200 to 350 for silicone antifoams used to produce SMC.

Silicone antifoams are hydrophobic, have low surface tension and low volatility. Studies have been conducted to demonstrate the synergistic effect of using a mixture of PDMS fluid and hydrophobic silica for use as an antifoam.⁵ Figure 2 provides a schematic of the interaction of the

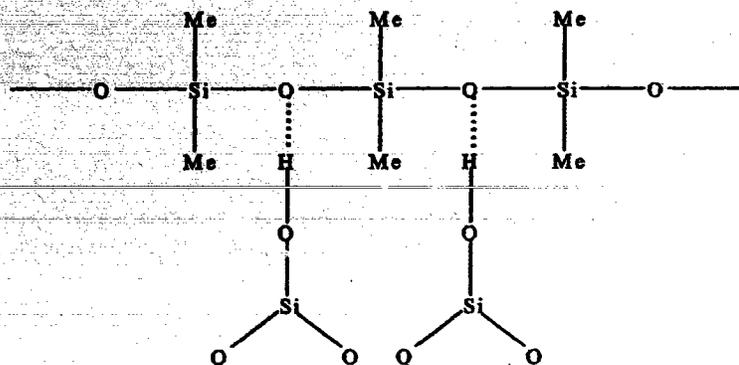


Figure 2. Proposed Schematic for the Interaction of PDMS with Silica

⁴ Hill, R. and Christiano, S.; "Antifoaming Agents", CRC Press, Inc. 1996

⁵ Degussa Technical Bulletin Pigments, "Synthetic Silicas for Defoamers", Bulletin No. 42

PDMS fluid with the silica that results in a silicone antifoam that is hydrophobic in nature which is essential for widespread distribution in an aqueous media.⁶

The manufacturing process for silicone antifoams is generally performed in a closed system with *local exhaust ventilation* (LEV) present, minimizing worker exposure to any dusts or chemicals that may be present.

Processing and Distribution Network:

Figure 3 provides a diagram of the processing and distribution network for silicone antifoams used in food processing. Food companies use antifoams as process aids to eliminate excessive foaming. In addition to food companies, antifoams are sold (directly or through distributors) to companies that blend these antifoams with other materials to make specialized antifoams. In turn, these companies (*antifoam formulators* in Figure 3) sell the specialized antifoams to food companies (directly or through distributors) for use as process aids.

Finally, silicone antifoams are sold to companies known as *food formulators*. These companies manufacture intermediate food products, such as yeast, -- used by food companies to make finished food products. Many food formulators have foaming problems similar to those experienced by food companies, and, like food companies, food formulators use silicone antifoams to eliminate excessive foaming. These products are sold to food companies (directly or through distributors) for use in making food products that are ready for sale to the public. See Appendix B for examples of applications using silicone antifoams in food processing.

Silicone antifoams for use in AF and/or AA products are sold directly to companies who produce these OTC products. The AF and AA products are manufactured into liquids, chewable tablets, drops and caplets under Good Manufacturing Practices (GMPs) as defined by the U.S. FDA.

⁶ R.D. Birtley, et al., "The effect of free silica on the mucosal protective and antifatulent properties of polydimethylsiloxane", J. Pharm. Pharmac., 1973, 25, 859-863

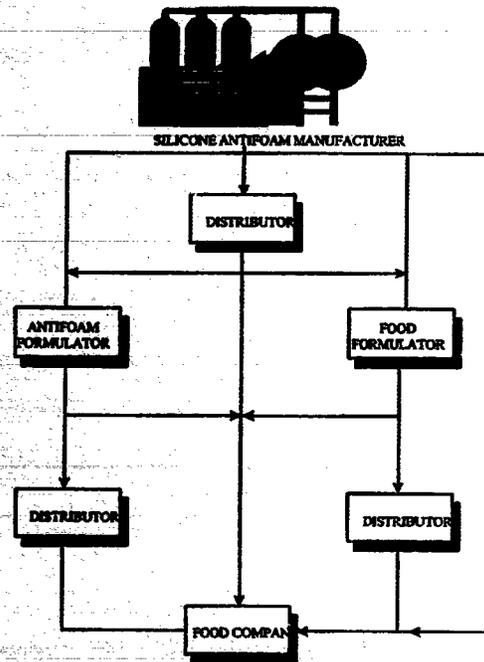


FIGURE 3. PROCESSING AND DISTRIBUTION NETWORK FOR ANTIFOAMS USED AS SECONDARY DIRECT FOOD ADDITIVES

Scope of the Analysis

As noted above, the study materials in this analysis include D₄, D₅, and D₆. These materials have distinct physiochemical properties and differing toxicological properties. For this reason, separate dose estimates are made for each of the study materials. Consumer exposure to the study materials is quantified using two-dose metrics:

- (i) The *average daily dose (ADD)*, expressed in milligrams (mg) of each of the study materials *per kilogram of body weight per day (mg/kg/day)* which averages the exposure over an extended period based on the amount consumed via food intake or usage of antigas products and the average food intake or reported frequency of use of these antigas products as determined from market surveys, and/or government sources.

- (ii) *the recommended maximum dose during use (RMDDU), specifically related to the use of antigas products for this study, is also expressed in units of mg/kg/day. The RMDDU limits the averaging period to the days during which the antigas product is actually being taken. The RMDDU is greater than the ADD because the RMDDU assumes daily use at the maximum recommended dosage, whereas the ADD may involve a lower dosage and is averaged over period of use and nonuse.*

The ADD measure is appropriate for a material with chronic (rather than acute) effects, whereas the RMDDU is more appropriate for a material that could produce an adverse effect with only limited temporal exposure. The RMDDU also provides a conservative upper bound to the ADD in cases where frequency-of-use data are not available. *Both the ADD and RMDDU exposure estimates reflect absorption through the GI tract and do not measure dose to any specific target organ.* Dose-to-target-organ calculations require additional data and/or models and are lower than those estimated here.

The key outputs of the exposure analysis for silicone antifoam products include: identification of relevant exposure pathways; description of consumer usage patterns; enumeration of exposed populations; and ADD and RMDDU calculations for the consumer population(s) under study.

Potential relevant subpopulations include: adults, the elderly, women of childbearing age, infants and children. Adult consumers include persons 18 years of age and older.

Summary of Key Findings

- Silicone Antifoams in General

- The route of exposure considered in this study is oral ingestion. Dow Corning Corporation (DCC) oral dosing studies using Fischer 344 rats estimated an absorption factor for D_4 in

PDMS fluid of 12.13%.⁷ This estimate is appropriate for D₄ in a PDMS fluid similar to that used in the manufacture of silicone antifoam products. The absorption factors for D₅ and D₆ are assumed to be identical to that of D₄, although it is likely the oral absorption for these two materials will be lower than it is for D₄. As additional testing is completed, the absorption factors used in the ADD and RMDDU calculations of D₅ and D₆ can be adjusted accordingly.

- Inhalation studies on laboratory rats to D₄ have shown adverse effects on certain reproductive parameters, however, the significance of these results to humans is unknown at this time.

- Silicone Antifoams in Food Processing

- For the purpose of calculating ADD estimates for D₄, D₅ and D₆ from the use of silicone antifoams in food processing EPA's Exposure factors handbook (Nov., 1995) was used to estimate daily food and liquid intake.
- The base case for exposure from the use of silicone antifoams in food processing is assumed to include the entire U.S. population as food consumption is not considered an elective variable.
- The level of PDMS allowable in food after the use of silicone antifoams is specified by the FDA in 21 CFR 173.40. The maximum allowable of 10 ppm PDMS was used as a default value.
- Chemical analysis of silicone antifoam used in food processing show an average D₄, D₅ and D₆ content of 4.9%, 3.2% and 1.0% respectively.⁸
- The ADD calculations for infants, children, and adults are conservative estimates based on the presence of silicone antifoams (PDMS) at a 10 ppm level in 50% by weight of the liquid (except water and milk) and solid food consumed on average daily. Fifty percent was used as a conservative estimate based on the low market share for silicone antifoams in the overall antifoam market segment in food processing.
- Male and female body weights (by age group) are estimated from EPA's Exposure Factors Handbook (Nov., 1995) for the purpose of estimating ADD's.

⁷ Crofoot, S. D., McMahon, J. M., Hubbell, B. G., Seaton, M. J., and Plotzke, K. (1997). Absorption and disposition of octamethylcyclotetrasiloxane in female Fischer 344 rats following delivery in two carriers via gavage. *The Toxicologist*, Vol. 36, No. 1, Part 2, p.143.

⁸ Dow Corning analysis of silicone antifoam product used in food processing.

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- The ADD's for D₄, D₅ and D₆ from the consumption of food that has been processed with silicone antifoams do not exceed .002 mg/kg/day, .001 mg/kg/day and .0004 mg/kg/day for infants respectively and .0007 mg/kg/day, .0005 mg/kg/day and .0002 mg/kg/day for adults.

- Silicone Antifoams in AA/AF Products

- According to published market research estimates, nearly one in two (48% of) adult Americans reported buying an AA or AF in the preceding six months ("users") and approximately one in five use AGs (AFs and AAs containing silicone antifoam). The number of adult consumers of AGs is conservatively estimated at 38.13 million (MM). Approximately the same percentage of men and women use AGs but, because there are more women than men in the U.S. population, women users account for approximately 55% of the consumer population.
- Although AG products are used to treat symptoms of colic in infants and also to treat symptoms of gas in children, there are no published estimates of the number of infants or children who use these products. Based on a conservative estimate of the percentage of infants with colic, an estimated 3.2 MM infants may be exposed to the study materials as a result of consumption of AGs. The number of children potentially exposed to the study materials is estimated as 8.87 MM. Counting adults, infants, and children, approximately 50.2 MM are potentially exposed to the study materials as a result of the use of AG products.
- On average, adult consumers are estimated to use AG products approximately 4.2 times per month. The frequency of use of these products ranges from zero times per month to nine or more times per month. In one major market research survey, AG consumers are partitioned into "light users" (0 to 2 times per month), "medium users" (3 to 7 times per month), and "heavy users" (8 or more times per month). In terms of the usual population subdivisions, there are only small differences in the relative proportions of light, medium, and heavy users as a function of gender (men versus women), race, ethnicity (white, black, Hispanic), or education. However, frequency of use varies with age, being highest among seniors. For example, among 18- to 24-year-olds, only 16% of consumers would be classified as heavy users, whereas among those over 65 years of age the percentage of heavy users doubles to approximately 32%. Proportionally more seniors (25.2% versus approximately 20%) are

exposed to these products and seniors tend to use these products with greater frequency than adults overall.

- A typical AG liquid formulation, extra strength, used by adults was analyzed to determine the concentrations of the study materials D₄, D₅ and D₆. Chemical results indicated average concentrations of D₄, 3.23 ppm; D₅, 3.78 and D₆, 2.26 ppm. This typical AG liquid formulation is used in the ADD and RMDDU calculations to assess potential exposures to D₄, D₅ and D₆ for the consumer populations identified.
- A typical representative AG liquid formulation used for the treatment of colic in some infants and by some children for symptoms of gas, was analyzed to determine the concentrations of the study materials D₄, D₅ and D₆. Chemical results indicated average concentrations of D₄, D₅, and D₆ are 2,698 ppm, 1,848 ppm and 620, respectively. This typical liquid formulation for infants/children is used in the ADD and RMDDU calculations to assess potential exposures to D₄, D₅ and D₆.
- The ADD's for D₄, D₅ and D₆ from using antigas products that contain silicone antifoams were calculated using both market research data to determine the frequency of use for adults and the maximum daily use as specified on the product label. The ADD's for D₄, D₅ and D₆ for adults do not exceed 1.72×10^{-5} mg/kg/day, 2.02×10^{-5} mg/kg/day and 1.21×10^{-5} mg/kg/day respectively based on frequency of use data from market research studies and 3.70×10^{-4} mg/kg/day, 4.33×10^{-4} mg/kg/day and 3.3×10^{-4} mg/kg/day assuming the maximum daily use as recommended on the product label.
- The ADD's for D₄, D₅ and D₆ for infants and children were calculated on a maximum daily use basis due to the lack of market research data on frequency of use. The estimated ADD's for D₄, D₅ and D₆ for infants do not exceed .12 mg/kg/day, .08 mg/kg/day and .028 mg/kg/day respectively and .147 mg/kg/day, .1 mg/kg/day and .034 mg/kg/day for children.

Exposure Pathways

Because D₄, D₅ and D₆ are present in such small or trace quantities (e.g., ppm) in silicone antifoam products, workplace and general population exposure to the study materials is expected to be *de minimis*. This exposure analysis considers only the oral ingestion pathway.

Identification and Estimation of Exposed Populations

This section provides information on the numbers of persons potentially exposed to the study materials as a result of consumption of food/liquid that has been processed with silicone antifoams or through the use of antigas products. It is based upon market research estimates and other relevant information. These estimates are described here. Separate estimates are developed for several potentially relevant subpopulations.

- Silicone Antifoams in Food Processing

The number of people who are potentially exposed to D₄, D₅ and D₆ through the use of silicone antifoams in food processing is not known, but as a conservative default the entire U.S. population is considered as the exposure group. The assumption is used that most food that is processed has some contact with silicone antifoams. In actual fact, silicone antifoams have a small share of the overall antifoam market. The ADD calculations considered 50% of the liquid (except water and milk) and solid food as having been processed with a silicone antifoam. The number of people who are exposed to D₄, D₅ and D₆ through food consumption is, in all likelihood, large but the actual exposure on a daily basis extremely low because most food will not have been processed using silicone antifoams based on the low market share for silicone antifoams.

- Antigas Product Use***- Adults***

Mediamark Research Incorporated (MRI), a major market research firm, provides consumption data for numerous consumer products including both AAs and AFs. MRI estimates are based on a large survey group of adults defined as those aged 18 or greater. MRI data are used to estimate the population of adults that use AGs. The size of the U.S. adult population (both men and women) in 1996 was estimated by MRI to total approximately 191,662,000. MRI (1996) estimated the number of adults who have used "indigestion aids and upset stomach remedies" (which include AGs and AAs not containing silicone antifoam) within the past six months as approximately 92,056,000, or 48% of the adult population. This estimate includes remedies (such as AA's) that do not contain silicone antifoam as well as those that do—so it is

necessary to eliminate users of AAs from this total. MRI provides brand-by-brand estimates (for the major brands) of the number of persons who have consumed indigestion aids and upset stomach remedies in the preceding six months ("users" as defined in this analysis). Numerous minor brands (including "store brands") are lumped into a category described as "other." Unfortunately, these brand-share data are regarded *confidential business information* (CBI) by MRI and cannot be provided in this document. However, it is possible to release the *aggregate* number of users of brands containing silicone antifoam. Adding together the estimated number of users of major brands containing silicone antifoam and assuming, conservatively, that all products included in the "other" category also contain silicone antifoam, results in an estimate of approximately 38,128,000 adults (20,914,000 women and 17,214,000 men) that use a silicone antifoam -containing product—approximately 20% of the U.S. adult population and 41% (38,128,000/92,056,000) of the population who reportedly use one or more indigestion aids and upset stomach remedies.

The estimate of 38.13 million adults is likely to *overstate* the number of U.S. adults who are exposed to silicone antifoam as a result of use of AGs because (i) some persons may have used more than one brand of AG in the preceding six months and are thus "double counted" in the MRI brand-specific estimates, and (ii) all brands in the "other" category are assumed to contain silicone antifoam, whereas many of these products in the "other" category may use conventional AAs that do not contain silicone antifoam. Nonetheless, 38.13 million persons is taken as a reasonable, albeit conservative, estimate.

--Infants

Infants are often identified as a subpopulation of interest out of concern for possible susceptibility. As well, infants have lower body weights than adults and might experience higher exposure on a mg/kg/day basis. MRI does not estimate the number of either infants or children using consumer products generally or these products in particular. Other methods have to be used for these groups.

Infants are defined herein as those less than two years of age. According to information available from the Bureau of the Census, there were approximately 8.0 million (Census of 1990) infants in the United States. The operative question is "how many of these infants are treated

with silicone antifoam -containing AGs?" As noted above, AGs are recommended for treatment of symptoms of colic in infants. The incidence of colic has been studied by several investigators. Estimates of the percentage of infants who experience colic range from 15% to 40%.⁹

-Children

Children are often identified as a separate subpopulation in exposure studies for the same reasons as infants. As noted above, MRI studies only the adult population, so an alternative basis for estimation is required for children. According to the 1990 Census estimates, there are approximately 57.2 million "children" (i.e., those from age 2 through age 17). As with infants, the operative question is: "how many of these children use AGs?" This age group does not experience symptoms of colic. However, labels on products intended for treatment of colic in infants also note that these can be used for relief from symptoms of gas in the digestive tract for children and adults. It is noted above that approximately 20% of adults are users of AGs. As noted below, however, the percentage of adults who consume AAs or AGs varies with age—being lowest for adults in the 18 to 24-year-old age group. According to MRI estimates, approximately 9.38 million out of 24.848 million persons in the 18 - 24-year-old group (37.7%) use AAs or AGs. Based on the overall ratio of AG/(AA plus AG) users of 41% calculated above, an estimated 15.5% (37.7% x 41%) of the 18 to 24 year-old age group use only AGs. Assuming that this proportion is the same for children, the estimated number of children exposed to the study materials through AG use is 8.87 million (15.5% x 57.2 million) children.

⁹ Estimates of the prevalence of colic in infants are available from a number of literature sources. Colic was found to range in prospective epidemiology studies from 8% to 26% and in the general pediatric population from 21% to 40% (see: Pinyerd, Belinda, J. and Zipf, William B. (1989). "Colic: idiopathic, excessive infant crying," *Journal of Pediatric Nursing*, Vol. 4, No. 3. Additional clinical studies showed as many as 15% to 40% of the infants experiencing symptoms related to colic (see: Pray, W. Seven. (March 1997). "Infant colic: the therapeutic puzzle," *U. S. Pharmacist*.)

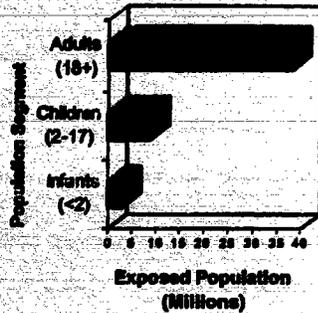


Figure 4. Estimated Populations Exposed to the Study Materials as a Result of Consumption of AG Products

- Total Exposed Population for Antigas Products

Based on these estimates, the exposed population for antigas products is conservatively estimated to total approximately 38.13 million adults plus 3.20 million infants plus 8.87 million children, or (since these categories are mutually exclusive and collectively exhaustive) – approximately 50.2 million persons in total. These estimates are summarized on Figure 4.

Relevant Dose Measures and Calculations

As noted above, the dose measure calculated in this report is the ADD. Calculation procedures for each are reviewed below. Product-specific calculations may be appropriate for product safety analysis but, for the purposes of an exposure analysis, it is appropriate to use “generic” products. Accordingly, three representative products are examined in this analysis: (i) a silicone antifoam for food processing with highest level of D₄, D₅ and D₆, (ii) a liquid extra-strength AG for adults and, (iii) a special infant/child AG formulation. The ADD is the average daily dose of the study materials expressed on a mg/kg/day basis. Figures 5 & 6 provide an overview of the computational logic for calculating the ADD for D₄, D₅ and D₆.

- Silicone Antifoams in Food Processing; ADD Computational Logic

Figure 5 is a diagram of the computational logic for calculating the ADD for the oral ingestion pathway from the use of silicone antifoam products in food processing. Key inputs for these calculations are the concentration of the study materials (e.g. D₄, D₅, D₆), concentration of silicone antifoam in food, average daily food consumption, oral absorption rate for the study materials, and body weight of the exposed subjects (e.g., infants, children and adults). Table I provides a summary of body weight and food consumption by age group. To understand the ADD calculations for the ingestion pathway for silicone antifoams in food processing, the following example is used (Basis: male adult, 18 - 45 years of age). The sum of the solid food

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and liquid intake for a male in the 18 - 45 year old age category is 1820 gms. This number is reduced by 50% to reflect that based on the low market share of silicone antifoams it is unlikely that the entire amount of food consumed in a day would be processed with a silicone antifoam. This assumption provides a more realistic, yet still conservative, estimate of the total intake of food and liquid that is potentially processed with a silicone antifoam. The total intake of 910 gms are multiplied by the fraction that is potentially D_4 , D_5 , and D_6 . In this case 10 ppm (the amount of silicone antifoam allowable in food) times the fraction of D_4 (4.9%), D_5 (3.2%) and D_6 (1%) in the silicone antifoam. The amount of D_4 , D_5 , and D_6 is then multiplied by 1000 (grams to milligrams) to reflect the amount of the study materials in mgs. This equates to .45 mgs D_4 , .29 mgs D_5 , and .09 mgs of D_6 . The frequency of use is considered daily so the above numbers are on a daily basis. The next step is to calculate the actual uptake of the study material. For this assessment, an oral absorption of 12.13% is used for D_4 , D_5 , D_6 . The uptake of D_4 , D_5 , and D_6 is calculated by multiplying the potential amount of D_4 , D_5 , and D_6 ingested by the absorption rate (12.13%). The calculated uptake is .05 mgs/day D_4 , .035 mgs/day D_5 , and 0.01 mgs/day D_6 . The ADD is then calculated by dividing the uptake by the body weight (for the age group and sex of the exposure group). In this case, the body weight is 75.9 kg. The ADDs are .0007 mg/kg/day D_4 , .0005 mg/kg/day D_5 and .0002 mg/kg/day D_6 . Table II contains a spread sheet of the ADD calculations for males and females by age category.

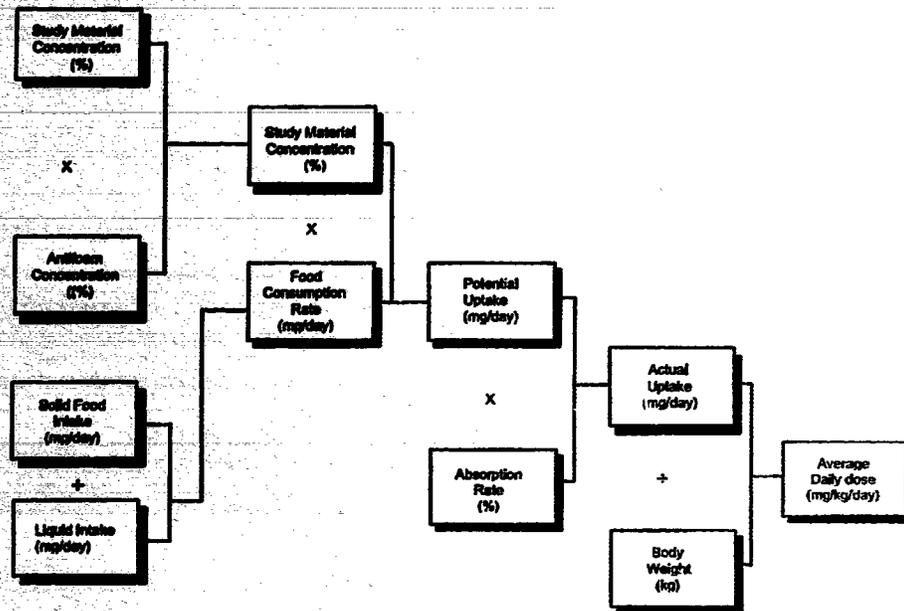


Figure 5. ADD Computational Logic for Silicone Antifoams in Food

– ADDs Resulting from the Use of Silicone Antifoams in Food Processing

The use of silicone antifoams in food processing provide low levels of exposure to D₄, D₅ and D₆. The ADD's for D₄, D₅ and D₆ from the consumption of food that has been processed with silicone antifoam do not exceed .002 mg/kg/day, .001 mg/kg/day and .0004 mg/kg/day for infants respectively and .0007 mg/kg/day, .0005 mg/kg/day and .0002 mg/kg/day for adults, based on an estimated oral absorption of approximately 12% for D₄, D₅ and D₆. These estimates assume that 50% of all food and liquids (except milk and water) are processed with silicone antifoams before human consumption. This is a very conservative estimate for quantifying the exposure through the use of silicone antifoams in food processing as the estimated market share for silicone antifoams in food processing is between 10 and 20%. This analysis provides a screening assessment to of the ADDs for D₄, D₅ and D₆ through the use of silicone antifoams in food processing.

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TABLE I. Default Assumption Values for Body Weight and Food/Liquid Intake

Age	Body Weight ⁹		Food and Liquid Intake					
	Male (kg)	Female (kg)	Nonmeat ¹⁰ (gm)	Meat ¹¹ (gm)	Dairy Products ¹² (gm)	Total Food (gm)	Liquid ¹³ (gm)	(Total Food and Liquid Intake) + 2 ¹⁴ (gm)
< 1	10.6	9.8	211	50	296.7	557.7	130	343.85
1 - 6	17.3	16	439	92	46	577	310	443.5
6 - 14	40	39	510.9	156	53.3	720.2	400	560.1
14 - 18	69.1	56.8	511.2	252	53	816.2	580	698.1
18 - 45	75.9	63.6	508.2	250	52	810.2	1010	910.1
45 - 75	78	67.3	515	250	55	820	780	800

⁹ US EPA Exposure Factors Handbook, Nov., 1995 (Draft), Table 5-2, 6-3
¹⁰ US EPA Exposure Factors Handbook, Table 2-75; includes produce, breads, cereal and other grain
¹¹ US EPA Exposure Factors Handbook, Table 2-84; includes meat, poultry and fish
¹² US EPA Exposure Factors Handbook, other dairy products excluding milk
¹³ US EPA Exposure Factors Handbook, Table 2-18; excluding water and milk
¹⁴ Total Liquid and Food Intake is divided in half to compensate for low market share of silicone antifoams

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Table II. Average Daily Dose for D₄, D₅ and D₆ from the Ingestion Pathway Associated with the Intake of Food Potentially Processed with Silicone Antifoams

Age Range (yr)	<1		1-6		6-14		14-18		18-45		45-75	
	Male	Female										
Sex												
Body Weight (kg)	10.6	9.8	17.3	16	40	39	69.1	56.8	75.9	63.6	78	67.3
Total Intake (gm/day)	344	344	444	444	560	560	698	698	910	910	800	800
Antifoam Content (ppm)	10	10	10	10	10	10	10	10	10	10	10	10
D ₄ Content in Antifoam (%)	4.9	4.9	4.9	4.9	4.9	4.9	4.9	4.9	4.9	4.9	4.9	4.9
D ₅ Content in Antifoam (%)	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
D ₆ Content in Antifoam (%)	1	1	1	1	1	1	1	1	1	1	1	1
D ₄ Oral Absorption (%)	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13
D ₅ Oral Absorption (%)	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13
D ₆ Oral Absorption (%)	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13	12.13
Average Daily Dose (ADD)												
D ₄ (mg/kg/day)	0.0019	0.0021	0.0015	0.0017	0.0008	0.0009	0.0006	0.0007	0.0007	0.0009	0.0006	0.0007
D ₅ (mg/kg/day)	0.0013	0.0014	0.001	0.0011	0.0005	0.0006	0.0004	0.0005	0.0005	0.0006	0.0004	0.0005
D ₆ (mg/kg/day)	0.0004	0.0004	0.0003	0.0003	0.0002	0.0002	0.0001	0.0002	0.0002	0.0002	0.0001	0.0001

- Silicone Antifoams in Antigas Products; ADD Computational Logic

Figure 6 provides a diagram of the computational logic for calculating the ADD for D_4 , D_5 and D_6 from the use of silicone antifoams in antigas products. It begins with the AG dosage of 5000 mg/teaspoon (tsp)¹⁵. Multiplying this quantity by the number of tsp per use (typically found on the label of the product) enables calculation of the AG (mg) dose per use. For example, if a product has a recommended dose of 2 to 4 tsp per use, the larger value, 4 tsp/use, is chosen as a conservative input to these computations. Multiplying 4 tsp/use by 5000 mg AG/tsp yields 20,000 mg AG per use.

Moving to the bottom of the schematic in Figure 6, frequency of use (uses per month) data are available from MRI. Dividing the frequency of use (interpreted as days on which the product is used) per month by the assumed number of days per month (30) results in a frequency of use per day. According to the data presented in Table III, AGs are estimated to be used on average approximately 4.2 times per month. (interpreted as 4.2 days per month), or $4.2/30$ equals 0.14 uses/day.

The product of the daily frequency of use (0.14 uses/day) and the AG dose/use is the daily use in mg of AG/day, or $(20,000 \text{ mg AG/use}) \times (0.14 \text{ uses/day}) = 2800 \text{ mg AG/day}$ in this example. The D_4 content of this product is 3.23 ppm. Therefore the potential uptake of D_4 per day is 2800 mg AG/day times $3.23 \times 10^{-6} \text{ mg } D_4/\text{mg AG} = 9.04 \times 10^{-3} \text{ mg } D_4/\text{day}$. However, only 12.13% of this amount is actually absorbed. The actual uptake is $(0.1213) \text{ times } (9.04 \times 10^{-3}) = 1.09 \times 10^{-3} \text{ mg } D_4/\text{day}$. This quantity, divided by the body weight of the consumer (75.9 kg in the case of an adult male) equals the ADD for D_4 ($1.45 \times 10^{-5} \text{ mg/kg/day}$ in this case). These computations are made for each of the study materials (see Table IV).

For women, the corresponding ADD for D_4 is slightly higher than that for men because of the lower average body weight of adult females compared to adult males.

¹⁵ A teaspoon for reference purposes is considered to be five milliliters (ml) by volume. Analysis by DCC has determined the average weight per volume of an AG product is approximately 1 gm/ml. Therefore a teaspoon of AG product is approximately 5 gms (or 5000 mg/teaspoon).

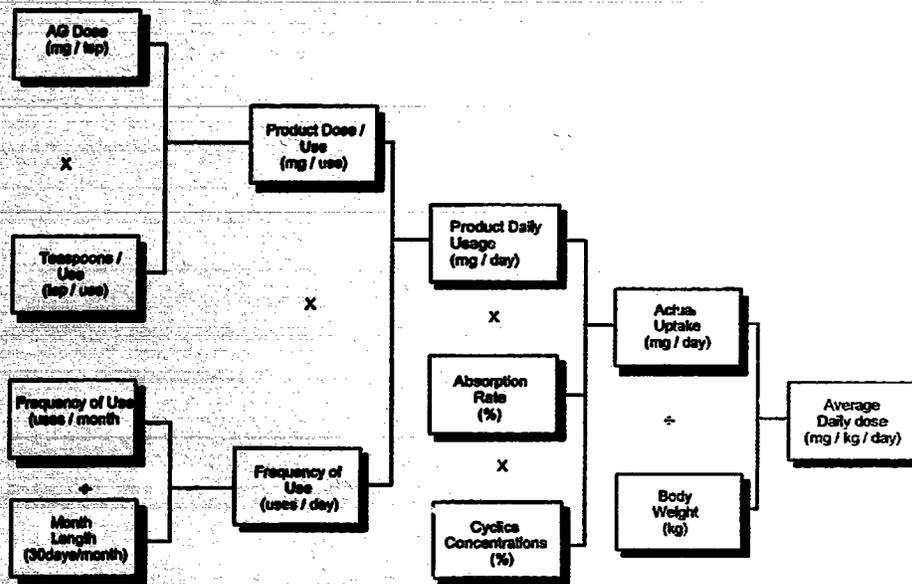


Figure 6. ADD Computational Logic for Silicone Antifoams in Antigas (AG) Products

- RMDDU

The ADD presents the daily dose (in mg/kg/day) averaged over periods of both use and nonuse. In the base case numerical example, AGs are used only 4.2 times per month—0.14 uses per day. On days when the product is used, the daily average would be substantially larger. Moreover, the product might be used more than once per day. For example, the label directions on extra-strength AG liquids recommends that the product be used no more than 3 times per day, i.e. (4 tsp/use x 3 uses/day = 12 tsp/day). If shorter term dose averages are required, it is necessary to modify the ADD computations. The RMDDU (recommended maximum dose during use) calculates the recommended maximum daily dose on those days when the AG product is used—not the average over a longer time period. Moreover, the RMDDU assumes that the product is taken several times (the recommended maximum) on the days when used. Thus, for

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practical purposes, the RMDDU is the ADD if it is assumed that the product is used the recommended maximum number of times each day.

These computations are shown in Table V and correspond to the ADD computations shown in Table IV. Obviously, the computed average doses are higher by a factor of 90/4.2 (=21.4).

It is interesting to note that the case depicted in Table V involves ingestion of 480 mg silicone antifoam per day - almost exactly the maximum daily dose permitted by FDA regulation. Thus, the RMDDU is a practical upper bound to the permitted ADD for this product.

Table III. Distribution of Frequency of Usage of AA/AG Products

<i>Times in Last 30 Days</i>	<i>Estimated User Population (000)</i>	<i>MRI User Category</i>	<i>Percent of User Population</i>	<i>Cumulative Percentage</i>	<i>Percent in User Category</i>	<i>User Category Average</i>
0	17,103	Light	18.6%	18.6%		
1	8,238	Light	8.9%	27.5%		
2	10,879	Light	11.8%	39.3%	39.3%	0.83
3	8,714	Medium	9.5%	48.8%		
4	9,309	Medium	10.1%	58.9%		
5	7,161	Medium	7.8%	66.7%		
6	5,417	Medium	5.9%	72.6%		
7	2,185	Medium	2.4%	75.0%	35.6%	4.48
8	1,891	Heavy	2.1%	77.0%		
9	21,160	Heavy	23.0%	100.0%	25.0%	8.92
Total	92,057			Mean	100.0%	4.16

Note: Last interval is nine or more times. This is assumed to be nine for computational purposes, which may understate the true arithmetic mean.

Source: First three columns from MRI, 1996.

-Base Case

Tables IV(ADD) and V (RMDDU) present "base case" average dose computations for adult men and women.

-Base Case Variants

All the reasonable variants to the base case for adults relate to ADD computations rather than RMDDU; assuming that the product labels are fixed and the FDA maximum remains unaltered. As noted, the computed average frequency might be biased low because of the cut-off at nine times per month used by MRI in reporting the data.¹⁶ In fact, the ADD varies directly with the assumed frequency of use (other factors held constant). Thus, if it is assumed that the average frequency of use were twice the base case figure of 4.2, the resulting ADD would be twice the base case value.

A potentially relevant variant of the base case value for adults is the senior population. As noted above, a greater percentage of seniors fall into MRI "heavy user" category and, as well, (according to EPA's *Exposure Factors Handbook*) seniors have slightly different body weights than the population at large. Accordingly, Table VI replicates the computations given in Table IV, except that the average frequency of use for heavy users is 8.92 (Table III) which is used as a bounding case and the body weights are adjusted to EPA's estimates for seniors. The computed ADDs are slightly more than twice the base case values.

No adjustments are necessary to computations in Table IV to account for women of childbearing age. These women may have a slightly lower frequency of use than that assumed in Table IV, because they are slightly younger than the average adult, but this is a second-order factor.

-Infants

AG products are used in the treatment of colic in infants. For this purpose, special liquid products have been created. The standard dose of these special products for infants is one drop of approximately 0.3 ml. The D₄, D₅ and D₆ content of this product is 2,698 ppm, 1,848 ppm, and 620 ppm, respectively. Label directions indicate that this product "may be taken" four times per day, and "must not exceed" 12 times unless under the care of a physician.

Infant body weights are provided in EPA's *Exposure Factors Handbook* and are 10.6 kg and 9.8 kg for infant boys and girls, respectively.

¹⁶ Recall, however, that the median frequency of use (which is unaffected by this bias) is only four uses/month.

No frequency-of-use data was available for infant users of these products. MRI provides data for adult consumers, only. In consequence, it is only possible to estimate the RMDDU, rather than ADD values. Table VII provides these calculations based upon the inputs described above assuming that the product is used 4 times per day, as recommended on the label. In terms of D_4 , D_5 and D_6 , the RMDDUs do not exceed .04, .027 and .009 mg/kg/day for infants, respectively. Table VIII provides an identical set of calculations, except that the daily frequency is increased to 12 times, rather than 4, to match the "do not exceed" language on the label. Resultant RMDDUs are, in consequence, three times higher.

It is difficult to calculate ADDs because of the lack of frequency-of-use data. Nonetheless, it is unlikely that the actual frequency of use of silicone antifoam containing products is as great as 30 times per month. Thus, the true, but unknown ADD is likely to be substantially smaller than the RMDDU calculated in Table VIII.

—Children

Children also use the infant/child formula. Doses received by children will differ from those received by infants for two principal reasons; (i) the individual dose size for children is 0.6 ml, rather than 0.3 ml, so the average amount of silicone antifoam received per day will be doubled, and (ii) children's body weights are substantially greater than those of infants. As with infants, there are no published frequency-of-use data for children, so only RMDDU computations can be made. Because actual usage frequencies are likely to be substantially smaller than four times per day, the ADDs are less than the RMDDUs.

Tables IX and X present RMDDU calculations based on the "may be taken" and "do not exceed" frequencies for boys. Tables XI and XII present the same information for girls. The patterns are similar to those seen with infant formulations. As a point of interest, differences between RMDDUs for boys and girls are quite small as body weights for male and female children are much closer to each other than those of adults. In terms of D_4 , D_5 and D_6 , the RMDDUs for D_4 , D_5 and D_6 do not exceed .147, .101 and .034 mg/kg/day, respectively, for children.

Conclusion

This exposure assessment study provides a conservative analysis of the exposure to D₄, D₅ and D₆ from the use of silicone antifoams in the processing of food and as an ingredient in antigas products for the treatment of indigestion and upset stomach. For the purpose of this study, because of their low market share compared to organic antifoams, it was assumed that fifty percent of the food and liquids ingested had been processed with silicone antifoams. Even with this artificially high level of food contact with silicone antifoams the average daily dose exposure to D₄, D₅ and D₆ was very low for infants, children and adults. ADD's for D₄, D₅ and D₆ do not exceed 002 mg/kg/day, .001 mg/kg/day and .0004 mg/kg/day, respectively, for infants and .0007 mg/kg/day, .0005 mg/kg/day and .0002 mg/kg/day for adults.

The estimation of the exposure to D₄, D₅ and D₆ from the use of silicone antifoams in antigas products consumed for the relief of indigestion and upset stomach was evaluated based on frequency of use data from market research studies, where available, and on the recommended use as provided on the product label. The ADD's calculated from the recommended use as provided on the product label assume that the individual is using the antigas product daily which overestimates the true ADD based on the normal use of these products. Market research indicates that 77% of adults use these products eight times or less in a thirty day period. This effectively reduces the average daily dose calculated based on the recommended use by a factor of 3.75. As there was no available market research data on the frequency of use for infants and children the recommended use as provided on the product label was used as the default for calculating the exposure to D₄, D₅ and D₆. The ADD's for D₄, D₅ and D₆ for adults do not exceed 1.72×10^{-5} mg/kg/day, 2.02×10^{-5} mg/kg/day and 1.21×10^{-5} mg/kg/day respectively based on frequency of use data from market research studies and 3.70×10^{-4} mg/kg/day, 4.33×10^{-4} mg/kg/day and 3.3×10^{-4} mg/kg/day assuming the maximum daily use as recommended on the product label. The ADD's for D₄, D₅ and D₆ for infants and children were calculated on a maximum daily use basis due to the lack of market research data on frequency of use. The estimated ADD's for D₄, D₅ and D₆ for infants do not exceed .12 mg/kg/day, .08 mg/kg/day and .028 mg/kg/day, respectively, and .147 mg/kg/day, .1 mg/kg/day and .034 mg/kg/day respectively for children. The ADD's calculated in this study provide an essential component for the risk assessment for D₄, D₅ and D₆ as trace materials in silicone antifoams used in food processing and

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antigas products. These ADD measurements are likely to decrease in the future as manufacturing of antigas products and other users of silicones antifoams switch to silicone antifoams that contain much smaller amounts of D₄, D₅ and D₆.

PRODUCT: Typical Extra-Strength Liquid AG Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Men Consumers	Women Consumers	
Ingestion	D ₄ content of product	ppm	3.23	3.23	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical liquid extra-strength AG product formulation
	D ₅ content of product	ppm	3.78	3.78	
	D ₆ content of product	ppm	2.26	2.26	
	Product dose	mg/tsp	5,000	5,000	Product dose as recommended by product label instructions
	Teaspoons/use	tsp/use	4	4	High-end dosage per product label instructions
	Product dose/use	mg/use	20,000	20,000	calculated from mg/tsp and tsp/use
	Frequency of use	uses/month	4.2	4.2	See Table III
	Frequency of use	uses/day	0.14	0.14	Uses/month ÷ 30days/month
	Daily product usage	mg/day	2,800	2,800	Uses/day times mg/use
	D ₄ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	Body Weight	kg	75.9	63.6	Adult body weight assumed
	Average Daily Dose	D ₄	mg/kg/day	1.45x10 ⁻³	1.72x10 ⁻³
D ₅		mg/kg/day	1.69x10 ⁻³	2.02x10 ⁻³	Calculated from above inputs
D ₆		mg/kg/day	1.01x10 ⁻³	1.21x10 ⁻³	Calculated from above inputs

Table IV. ADD Calculations for Ingestion Pathway Associated with Adult Consumption of an AG Product -- Adult Users

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PRODUCT: Typical Extra-Strength Liquid AG Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Men Consumers	Women Consumers	
Ingestion	D ₄ content of product	ppm	3.23	3.23	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical liquid extra-strength AG product formulation
	D ₅ content of product	ppm	3.78	3.78	
	D ₆ content of product	ppm	2.26	2.26	
	Product dose	mg/tsp	5,000	5,000	Product dose as recommended by product label instructions
	Teaspoons/use	tsp/use	4	4	High-end dosage per product label instructions
	Product dose/use	mg/use	20,000	20,000	calculated from mg/tsp and tsp/use
	Frequency of use	uses/month	90	90	RMDDU assumption
	Frequency of use	uses/day	3	3	Uses/month ÷ 30days/month
	Daily product usage	mg/day	60,000	60,000	Uses/day times mg/use
	D ₄ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	Body Weight	kg	75.9	63.6	Adult body weight assumed
	RMDDU	D ₄	mg/kg/day	3.10x10 ⁻⁴	3.70x10 ⁻⁴
D ₅		mg/kg/day	3.62x10 ⁻⁴	4.33x10 ⁻⁴	Calculated from above inputs
D ₆		mg/kg/day	2.17x10 ⁻⁴	3.30x10 ⁻⁴	Calculated from above inputs

Table V. RMDDU Calculations for Ingestion Pathway Associated with Adult Consumption of an AG Product – Adult Users

PRODUCT: Typical Extra-Strength Liquid AG Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks	
			Men Consumers	Women Consumers		
Ingestion	D ₄ content of product	ppm	3.23	3.23	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical liquid extra-strength AG product formulation	
	D ₅ content of product	ppm	3.78	3.78		
	D ₆ content of product	ppm	2.26	2.26		
	Product dose	mg/tsp	5,000	5,000	Product dose as recommended by product label instructions	
	Teaspoons/use	tsp/use	4	4	High-end dosage per product label instructions	
	Product dose/use	mg/use	20,000	20,000	calculated from mg/tsp and tsp/use	
	Frequency of use	uses/month	8.92	8.92	For heavy users, see Table III	
	Frequency of use	uses/day	0.30	0.30	Uses/month ÷ 30days/month	
	Daily product usage	mg/day	6,000	6,000	Uses/day times mg/use	
	D ₄ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text	
	D ₅ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text	
	D ₆ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text	
	Body Weight	kg	78	67.3	Senior body weight taken from EPA Exposure Factors Handbook	
	Average Daily Dose	D ₄	mg/kg/day	3.01x10 ⁻³	3.49 x10 ⁻³	Calculated from above inputs
		D ₅	mg/kg/day	3.53x10 ⁻³	4.09x10 ⁻³	Calculated from above inputs
D ₆		mg/kg/day	2.11x10 ⁻³	2.41 x10 ⁻³	Calculated from above inputs	

Table VI. ADD Calculations for Ingestion Pathway Associated with Consumption of an AG Product -- Elderly Users

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PRODUCT: Typical Infant Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Male Infant Consumers	Female Infant Consumers	
Ingestion	D ₄ content of product	ppm	2698	2698	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical Infant Drop AG product formulation
	D ₅ content of product	ppm	1848	1848	
	D ₆ content of product	ppm	620	620	
	Product dose	mg/dose	300	300	Product dose as recommended by product label instructions (0.3 ml)
	dose/use		1	1	Representative product label instructions
	Product dose/use	mg/use	300	300	calculated from mg/drop and drops/use
	Frequency of use	uses/day	4	4	Product label - "may be taken" language
	Daily product usage	mg/day	1200	1200	Uses/day times mg/use
	D ₄ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	Body Weight	kg	10.6	9.8	Average <1 year old, EPA <i>Exposure Factors Handbook</i>
	RMDDU	D ₄	mg/kg/day	.037	.04
D ₅		mg/kg/day	.0254	.027	Calculated from above inputs
D ₆		mg/kg/day	.0085	.009	Calculated from above inputs

Table VII. RMDDU Calculations for Ingestion Pathway for Infant Usage of AG Drop Formula as per label "may be taken" language

PRODUCT: Typical Infant Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Male Infant Consumers	Female Infant Consumers	
Ingestion	D ₄ content of product	ppm	2698	2698	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical Infant Drop AG product formulation
	D ₅ content of product	ppm	1848	1848	
	D ₆ content of product	ppm	620	620	
	Product dose	mg/dose	300	300	Representative value for infant formula (0.3 ml)
	Dose/use		1	1	Representative product label instructions
	Product dose/use	mg/use	300	300	calculated from mg/drop and drops/use
	Frequency of use	uses/day	12	12	Product label - "do not exceed" language
	Daily product usage	mg/day	3600	3600	Uses/day times mg/use
	D ₄ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%	12.13	12.13	Fraction absorbed - estimate given in text
	Body Weight	kg	10.6	9.8	Average < 1 year old, EPA <i>Exposure Factors Handbook</i>
	RMDDU	D ₄	mg/kg/day	.111	.12
D ₅		mg/kg/day	.076	.082	Calculated from above inputs
D ₆		mg/kg/day	.026	.028	Calculated from above inputs

Table VIII. RMDDU Calculations for Ingestion Pathway for Infant Usage of AG Drop Formula as per label "do not exceed" language

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PRODUCT: Typical Infant - Children's Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Boy	Consumers	
Ingestion	D ₄ content of product	ppm	2698		Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical Infant - Children's Drop AG product formulation
	D ₅ content of product	ppm	1848		
	D ₆ content of product	ppm	620		
	Product dose	mg/dose	600		Representative value for infant formula (0.6 ml)
	Dose/use			1	Representative product label instructions
	Product dose/use	mg/use	600		calculated from mg/drop and drops/use
	Frequency of use	uses/day		4	Product label - "may be taken" language
	Daily product usage	mg/day		2400	Uses/day times mg/use
	D ₄ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	Age	Years	1 - 6	6 - 14	
	Body Weight	kg	17.3	40	body weights taken from EPA Exposure Factors Handbook
RMDDU	D ₄	mg/kg/day	.045	.02	Calculated from above inputs
	D ₅	mg/kg/day	.031	.013	Calculated from above inputs
	D ₆	mg/kg/day	.01	.005	Calculated from above inputs

Table IX. RMDDU Calculations for Ingestion Pathway for Male Children's Usage of AG Drop Formula as per label "may be taken" language

PRODUCT: Typical Infant - Children's Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Boy Consumers		
Ingestion	D ₁ content of product	ppm	2698		Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical Infant - Children's Drop AG product formulation
	D ₂ content of product	ppm	1848		
	D ₃ content of product	ppm	620		
	Product dose	mg/dose	600		Representative value for infant formula (0.6 ml)
	dose/use		1		Representative product label instructions
	Product dose/use	mg/use	600		Calculated from mg/drop and drops/use
	Frequency of use	uses/day	12		Product label - "do not exceed" language
	Daily product usage	mg/day	7200		Uses/day times mg/use
	D ₁ oral absorption	%	12.13		Fraction absorbed - estimate given in text
	D ₂ oral absorption	%	12.13		Fraction absorbed - estimate given in text
	D ₃ oral absorption	%	12.13		Fraction absorbed - estimate given in text
	Age	Years	1-6	6-14	
	Body Weight	kg	17.3	40	body weights taken from EPA Exposure Factors Handbook
RMDUU	D ₁	mg/kg/day	.136	.06	Calculated from above inputs
	D ₂	mg/kg/day	.093	.04	Calculated from above inputs
	D ₃	mg/kg/day	.0313	.014	Calculated from above inputs

Table X. RMDDU Calculations for Ingestion Pathway for Male Children's Usage of AG Drop Formula as per label "do not exceed" language

PRODUCT: Typical Infant - Children's Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
				Girl Consumers	
Ingestion	D ₄ content of product	ppm		2698	Composition for D ₄ , D ₅ , and D ₆ is based on DCC's chemical analysis of typical Infant - Children's Drop AG product formulation
	D ₅ content of product	ppm		1848	
	D ₆ content of product	ppm		620	
	Product dose	mg/dose		600	Representative value for infant formula (0.6 ml)
	Dose/use			1	Representative product label instructions
	Product dose/use	mg/use		600	calculated from mg/drop and drops/use
	Frequency of use	uses/day		4	Product label - "may be taken" language
	Daily product usage	mg/day		2400	Uses/day times mg/use
	D ₄ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	Age	Years	1-6	6-14	
	Body Weight	kg	16	39	body weights taken from EPA Exposure Factors Handbook
RMDUU	D ₄	mg/kg/day	.05	.02	Calculated from above inputs
	D ₅	mg/kg/day	.034	.014	Calculated from above inputs
	D ₆	mg/kg/day	.01	.005	Calculated from above inputs

Table XI. RMDDU Calculations for Ingestion Pathway for Female Children's Usage of AG Drop Formula as per label "may be taken" language

PRODUCT: Typical Infant - Children's Drop Formulation

Exposure Pathway	Quantity Estimated or Input	Units	Value		Source/Basis/Remarks
			Girl Consumers		
Ingestion	D ₄ content of product	ppm	2698		Composition for D4, D5, and D6 is based on DCC's chemical analysis of typical Infant - Children's Drop AG product formulation
	D ₅ content of product	ppm	1848		
	D ₆ content of product	ppm	620		
	Product dose	mg/dose	600		Representative value for infant formula (0.6 ml)
	dose/use			1	Representative product label instructions
	Product dose/use	mg/use	600		Calculated from mg/drop and drops/use
	Frequency of use	uses/day		12	Product label - "do not exceed" language
	Daily product usage	mg/day	7200		Uses/day times mg/use
	D ₄ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₅ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	D ₆ oral absorption	%		12.13	Fraction absorbed - estimate given in text
	Age	Years	1-6	6-14	
	Body Weight	kg	16	39	body weights taken from EPA Exposure Factors Handbook
RMDDU	D ₄	mg/kg/day	.147	.06	Calculated from above inputs
	D ₅	mg/kg/day	.101	.041	Calculated from above inputs
	D ₆	mg/kg/day	.034	.014	Calculated from above inputs

Table XII. RMDDU Calculations for Ingestion Pathway for Female Children's Usage of AG Drop Formula as per label "do not exceed" language

Appendix A - Food Additive Definition

A *food additive* includes any substance expected to become a component of food or affect the characteristics of food, including materials that migrate into food as a consequence of contact with packaging materials or process equipment as well as materials that are intentionally added to food. Several materials are specifically excepted, including pesticides, color additives, and new animal drugs. *Direct food additives* are materials that are added to food, and are intended to have a specific effect on properties or characteristics of the food itself. Examples include flavoring agents and fillers added to increase the fiber content of the food. *Secondary direct food additives* are materials that are added to food and intended to affect the *processing* of the food as opposed to the properties and characteristics of the food itself. These materials may also have effects on the properties and characteristics of the food, but are intended as process aids, and so are classified as secondary direct instead of direct food additives. The intended effect determines whether additives should be classified as direct or secondary direct. Examples of secondary direct additives include defoaming agents and chemicals used in washing or to assist in peeling' of fruits and vegetables. Silicone antifoams-excluding pulp and paper applications-fall into this category. Finally, *indirect additives* are materials that are not directly added to food, but are known (or may have potential) to migrate into food as a result of contact or proximity to packaging materials or processing, handling, and storage equipment (including food cooking hardware and appliances). Migration into food is not intended but if it occurs is subject to limits and regulations. This category includes materials that are intended to modify characteristics or properties of a material that may come into contact with food. These materials may, if they migrate into food, also affect characteristics or properties of food. Examples of materials that fall into this category include components of paper food packaging materials, components of coatings used on food packaging materials, lubricants and sealants in food processing equipment.

Appendix B - Silicone Antifoam Applications

Product Applications:

Excessive foaming creates problems in many stages of food and beverage processing. The foam that is generated occupies space in equipment that would otherwise be used to make product, reducing the usable capacity, hence throughput, of the processing equipment. If left uncontrolled, foam would spill out of processing equipment and onto floors, resulting in safety and sanitation problems and requiring periodic shut downs to clean up excess foam.

Foam is created when materials such as sugars, starches, or other organics typically found in foodstuffs are mixed in water and agitated. The mixture of materials in water causes a large variance in surface tension; thereby enhancing foam formation (*definition of foam, a large volume of gas is dispersed in a small amount of liquid*). Thus, when foam forms, a small volume of liquid is transformed into a much larger volume of foam. Foam is difficult to contain once it forms. If preventive measures are not taken, such as the use of antifoams, the process must be run at reduced throughput, and process vessels cannot be fully utilized because space must be dedicated to contain foam and prevent spilling out. Also, excessive foaming during processing can result in inefficient and incomplete mixing and impaired heat transfer which, in turn, can adversely affect the quality of the final product. Several specific examples of applications for silicone antifoams are summarized below:

- **Maple Syrup Processing** - Silicone antifoams are added to maple syrup blending tanks to eliminate foaming and to allow the tank to be used at full capacity. Eliminating foam that could easily billow over the top of the tank also eliminates the chance of a slippery, sticky, mess on the floor and loss of syrup. Use of antifoams provides additional capacity, avoids loss of product, and eliminates the need for labor to clean up foam overflows. A potential safety hazard is eliminated as well as workers could slip and become injured as a result of slippery foam on walkways.
- **Canned Fruit Processing** - In a typical fruit canning operation, the fruit is peeled, washed in a caustic soda solution, and cut before it is canned. The washing step is

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designed to remove impurities such as fertilizers and insecticides from the surface of the fruit. However, these impurities cause severe foaming in the fruit bath. Foaming causes the conveyor (which carries the fruit through the process) to become clogged, and slows the entire process down. When silicone antifoams are added in the washing process, foaming is dramatically reduced, allowing for greater capacity in the wash tank, and increased throughput. At one plant, the use of silicone antifoams allowed the amount of fruit processed in an eight-hour day to be *doubled*.

- **Sugar-Free Beverage Processing** - Sugar-free beverage manufacturers experience foaming problems when mixing ingredients that eventually become sugar-free soft drinks. Water, saccharin, cellulose, citric acid, and other ingredients are mixed in tanks, and heated. Foaming occurs when the temperature of the mixture rises above 100°F. This foaming gives rise to potential spills, safety hazards, and reduced capacity in the tanks. Silicone antifoams are added to the mixing tanks to minimize this problem. One beverage company increased the usable capacity of mixing tanks by *one-third* when antifoams were used to combat foaming problems.
- **Potato Chip Making** - Foaming occurs at several stages of the potato chip making process. The process consists of several steps: raw potatoes are "brush washed," peeled, sliced, and washed prior to frying and packaging. Water is used in the brush washing of raw potatoes to remove dirt and other foreign materials; water is also used in washing sliced potatoes to remove surface starch prior to frying (surface starch results in undesirable brown spots on the chips if not removed). Both of these washing processes generate thick foam because of starch that is washed off the potatoes. Any dirt that is in the wash water also becomes suspended in the foam, which tends to spill out over processing equipment and onto the floor, leading to safety and sanitation problems. Silicone antifoams are added to the wash water to control these foaming problems. One plant reported that nearly all visible foam was eliminated by using a silicone antifoam; cost and maintenance savings were estimated at 60% (this particular plant had previously been using an organic antifoam; presumably, savings would have been even greater if the base case had been with no

antifoam use). A second case study of a potato chip application points to another advantage of antifoams. This particular plant uses antifoams for foam control, and reports that as an added benefit, the antifoam makes it easier to recover high-grade starch from the wash water. This starch is sold to a nearby wood products firm for use in making paper. In this case the sale of the starch pays for the antifoam, and the labor required to recover the starch. Thus, this plant has eliminated foaming, improved plant cleanliness, and cut maintenance costs, all at an essentially zero net cost, and at the same time relieved the local water treatment plant of the burden of handling high-starch waste water.

Standard Industrial Classification (SIC) Codes:

Antifoams are used in a wide variety of food processing industries, including industries that fall under SIC Industry Groups 201 (meat products), 202 (dairy products), 203 (canned, frozen, and preserved fruits, vegetables, and food specialties), 205 (bakery products), 206 (sugar and confectionery products), and 208 (beverages). Table XIII contains a list of the SIC codes and descriptions of industries that are included in these Industry Groups.

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SIC CODE	DESCRIPTION
201	Meat Products
2011	meat packing plants
2013	sausages and other prepared meat products
2015	poultry slaughtering and process
202	Dairy Products
2021	creamery butter
2022	natural, processed, and imitation cheese
2023	dry, condensed, and evaporated dairy products
2024	ice cream and frozen desserts
2026	fluid milk
203	Canned, Frozen, and Preserved Fruits, Vegetables, and Food Specialties
2032	canned specialties
2033	canned fruits, vegetables, preserves, jams and jellies
2034	dried and dehydrated fruits, vegetables, and soup mixes
2035	pickled fruits and vegetables, vegetable sauces and seasonings, and salad dressings
2037	frozen fruits, fruit juices, and vegetables
2038	frozen specialties, not elsewhere classified
205	Bakery Products
2051	bread and other bakery products except, cookies and crackers
2052	cookies and crackers
2053	frozen bakery products, except bread
2087	flavoring extracts and flavoring syrups, not elsewhere classified
206	Sugar and Confectionery Products
2061	cane sugar, except refining
2062	cane sugar, refining
2063	beet sugar
2064	candy and other confectionery products
2066	chocolate and cocoa products
2067	chewing gum
2068	salted and roasted nuts and seeds
208	Beverages
2082	malt beverages
2083	malt
2084	wines, brandy, and brandy spirits
2085	distilled and blended liquors
2086	bottled and canned soft drinks and carbonated waters
2087	flavoring extracts and flavoring syrups, not elsewhere classified

TABLE XIII - SIC Codes for Companies that could use Silicone Antifoams as Secondary Direct Food Additives.

Advantages and Disadvantages of Silicones and Alternative Materials:

Alternative materials that might be used in place of silicone antifoams are primarily organic antifoams, such as organic oils, vegetable oils, fish oils, and stearate-based waxes. Silicone antifoams have a number of advantages over these materials, as described below.

In some applications silicone antifoams are unique, and there are no suitable substitutes. Examples of this type of application are powdered beverage and iced tea mixes. These products tend to generate a large amount of foam when mixed with water; adding silicone antifoams helps to eliminate this problem. Given presently available foam control technology, if silicone antifoams are not used in these applications the only choice is to live with the foam.

In general, silicone antifoams perform significantly better than organic antifoams; this gives silicones several advantages over alternate antifoams. First, silicones reduce foaming to a greater degree than do organic antifoams. This allows processes to be operated at closer to design maximum throughput rates, and allows more complete use of process equipment capacities. This also improves plant sanitation and safety by preventing foam from billowing out of process equipment and onto floors. Second, because silicone antifoams are five to ten times as effective as organic antifoams in secondary direct applications, silicones can be used at correspondingly lower levels. Third, silicones have a low affinity for water and organic materials in foods, and so they tend to stay on the surface of the foaming medium for a longer period of time; organic antifoams tend to lose effectiveness as they emulsify into the system and become part of the foaming medium. In washing processes such as the potato chip example discussed above, this means that silicone antifoams remain effective longer (less frequent antifoam additions are necessary), and a smaller amount of the antifoam actually remains on the food after processing. Finally, silicone antifoams have a greater temperature range of thermal stability than organic antifoams, and so can be used in cold-temperature applications such as frozen deserts, as well as applications where products are heated, such as jams and jellies.

Silicone antifoams also have several advantages over organic antifoams that are not directly related to performance as antifoams. Silicone antifoams have no noticeable smell or taste, add very few calories and little or no fat and cholesterol to foods, and are colorless. Organic antifoams, on the other hand, do have tastes and odors (particularly fish oils), which are

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incorporated into the foods in which they are used. Some organic antifoams contain calories, fat, and cholesterol, which are also incorporated into the food product.

As consumer preferences shift toward low-fat and low-cholesterol foods, the food industry is driven to remove more and more of the fatty organic materials that act as natural antifoams. This increases the foaming problems that must be solved, preferably without adding back calories, fat, and cholesterol.