

# Preservatives

David C. Steinberg, FRAPS  
Steinberg & Associates, Inc.  
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# Who Cares About Preservatives?

- They are all toxic
- They are all dangerous pesticides
- They are associated with every disease known to mankind
- They are chemicals
- They are unnatural
- They add costs with no benefit
- Hey, I can sell more of my product calling it “preservative free”.

# Because of This Mentality We Are Losing All of Our Preservatives

- Marketing and NGO's will never be satisfied.
- All the preservatives used in cosmetics have long history of safe use.
- Complaints about cosmetic injuries and more specifically, preservatives are very few.
  - Although the real facts are unknown
- We are now seeing a significant increase in recalls due to microbial contamination

# Definition

Preservation is the prevention or retardation of product deterioration from the time of manufacture until the product is used up by the consumer. This deterioration is due to microorganisms.

Diseases can be spread by contaminated cosmetics

Microbial contamination is adulteration as defined by the FDA

# What is a Preservative?

- **Chemical agents added to products to prevent the growth and to destroy microorganisms.**
- We add these to “clean” products to prevent deterioration by consumers under normal and foreseeable use conditions.
- We establish the adequacy of preservation by running an appropriate preservative efficacy or challenge test (PET).

# Challenge Testing (PET)

- A short term *in vitro* test to see if our product is adequately preserved.
- Works well for “typical” products but not for “atypical” cosmetics.
  - Typical cosmetics have water as the continuous phase or are aqueous solutions.
  - Atypical cosmetics have low water content or are anhydrous or do not have water as the external phase of an emulsion.

# FDA REGULATIONS-ADEQUACY OF PRESERVATION

- Cosmetics (and topical drugs) need not be sterile.
- They cannot be contaminated with pathogenic microorganisms and other organisms must be low.
- There must be sanitary storage and handling of raw materials and finished goods to prevent adulteration including microbial contamination.

# Recommendations

- **Each batch of a cosmetic which is not self-preserving, be tested for microbial contamination before it is released for interstate shipment, and**
- Each cosmetic, particularly each eye area cosmetic, be tested during product development for adequacy of preservation against microbial contamination which may occur under reasonably foreseeable conditions of consumer use.



# Reality

- We add preservatives to correct cGMP failures in production.
  - Why use pure strains in PET?
  - Why use “house” organisms?
  - How do you know if your preservative is working or you manufactured under cGMP’s ?
  - We call contamination of a finished product “a preservative failure”.
  - The FDA rejects post production sterilization for finished products.
    - Not applicable for ingredients

# Regulations

- Various countries regulate preservatives differently
  - US only prohibits, does not pre-approve
  - EU pre-approves by placing them on Annex V
    - **If it is not on Annex V, it can't be a preservative (LOL)**
  - Japan pre-approves by type of end product
  - Canada has a “hot list”
    - Prohibited chemicals
    - Restricted chemicals

# United States

- FDA has banned or restricted some preservatives
  - Mercury (21 CFR 700.13)
  - Hexachlorophene (21 CFR 250.250)
  - Bithionol (21 CFR 700.11)
  - Halogenated Salicylanilides (21 CFR 700.15)
- CIR reviews the safety of preservatives

# Unsafe or Insufficient Data

- Benzylparaben
- Chloroacetamide
- Sodium Iodate
- Glutural for leave-on products
- Bronopol & Bonodox in combination with amines that could form nitrosamines
- Formaldehyde in aerosols
  
- Also, the manufacturer of Dimethoxane has ceased recommending the use of this in cosmetics and had discontinued production..

# Canada Hot List-Prohibited

- Mercury & its compounds
- Hexachlorophene
- Bithionol
- Halogenated Salicylanilides
- Captan
- Chloramine T
- Dimethoxane
- Chloracetamide

# Canada Hot List-Restricted

- 2-Bromo-2-Nitro-1,3 Diol 0.1%
- 5-Bromo-5-Nitro- 1,3 Dioxane 0.1%
- Benzalkonium Chloride 0.1%
- Benzethonium Chloride 0.2% leave-on, 0.3% rise off
- Boric Acid and its salts 5%
- Chlorhexidene & salts 0.14% as free base
- Formaldehyde 0.2% as a preservative
- MIT products 0.01%-now not allowed in leave-on
- MCI/MIT 0.0015% rinse-off, 0.00075 leave-on
- Silver 0.04%
- Triclosan 0.3%

All have warnings and conditions of use

# EU Prohibited List

- Hexachlorophene
- Bithionol
- Halogenated Salicylanilides
- Captan
- Dimethoxane
- Sodium Pyrithione
- Isopropyl Paraben (not supported)
- Isobutylparaben (not supported)
- Benzylparaben (not supported)
- Quaternium-15

# European Union

- Preservatives must be pre-approved and placed on Annex V
- Maximum levels, restrictions and mandated warnings
  - All warnings must be in all languages
- Transparent system to be approved
  - Time consuming and expensive
- Currently requires animal testing
  - Conflicts with other regulations



# European Union (continued)

- They have reviewed all preservatives which use to have “+” signs allowing for higher uses for other purposes in older regulations
- They have than listed these in Annex III
- Now all cosmetics must have the results of a challenge test in their Cosmetic Safety Report
  - Does this make sense?

# European Union (continued)

- 'Salts' is taken to mean: salts of the cations sodium, potassium, calcium, magnesium, ammonium and ethanolamines; salts of the anions chloride, bromide, sulphate, acetate.
- 'Esters' is taken to mean: esters of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, phenyl.
- All finished products containing formaldehyde or substances in this Annex and which release formaldehyde, must be labeled with the warning 'contains formaldehyde' where the concentration of formaldehyde in the finished product exceeds 0.05 %.
  - By the EU method

# In the EU they define pathogens:

- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*
- *Candida albicans*

# Other Requirements

- All Cosmetics must have micro specifications
- All raw materials must have micro specifications
- All products with more than 30 months stability must have “period after opening” symbols
  - Preservation challenge testing is the key (?)
  - Exceptions are aerosols, unit dose products, and products which can never change or support micro growth (prove this!)
    - Water activity is allowed as a PET method if below 0.6

# Japan

- 4/1/2001 Change their cosmetic regulations with a positive list for preservatives
  - Use allowed in all cosmetics (1)
  - Limited use in rinse-off products, no mucous contact(2)
  - Leave-on, no mucous membrane contact(3)
  - Rinse-off & leave-on with mucous membrane contact(4)
- Since then several new preservatives have been approved
- Quasi-drugs still required a CLS listing and pre-approval

# Japanese

(allowed in all cosmetics)

• Sodium Benzoate	1.0
• Salicylic acid	0.2
• Sodium Dehydroacetic acid	0.5
• Sorbic acid & salts	0.5
• Triclosan	0.1
• Parabens	1.0 total
• Phenoxyethanol	1.0
• Polyaminopropyl Biguanide	0.1

# Japanese

(allowed in rinse-off & leave-on no mucous contact)

- Chlorphenesin 0.3
- TCC no limit
- MCI & MI 0.1 as sold
- DMDM Hydantoin\* 0.3
- Imidazolidinyl Urea\* 0.3
- MIT 100 ppm
- Iodopropynyl Butylcarbamate 200 ppm

\* Required warning: "Should not be used by infants or by people who are hypersensitive to formaldehyde"

# Acceptable Microbial Limits

- General use cosmetics: Less than 1,000 ( $10^3$ )  
cfu/mL
- Eye area and baby products: Less than 100 ( $10^2$ )  
cfu/mL
- There must be no detectable pathogens present.



# 2011

- FDA had hearings in late November, 2011 on this.
- May come out with new guidelines (? Still waiting!)
- Significant import detentions over this!
  - What are objectionable organisms?
  - What levels are allowed?
  - All caused by 1 cfu/mL of *B. cereus*

## ***B. cereus***

- Bacillus cereus is a Gram positive rod
- Found in soil and on our body
- Causes illness by ingestion
- Before 2011 was not considered an objectionable organism

# Common Test Method

- USP <61> Microbial Limits Test
  - A recovery analysis is performed to verify that microorganisms present in a sample can be adequately plated/recovered on the chosen agar medium.
  - An aliquot of test specimen is dissolved in phosphate buffer (additional media containing emulsifying agents and/or surfactants may also be used).
  - 1 mL of the suspension is plated over agar plates and incubated.
  - Microbial colonies are totaled and expressed as either CFU/g or CFU/mL of test specimen.

# Why is this so Important?

- All recalls of contaminated cosmetics, occurred because companies shipped contaminated products.
- Why didn't they test?
- I know my preservative system is working and all the bugs will die off

Or

- Marketing needed the product shipped.....

# **FORMULATING WITH PRESERVATIVES**

- 1. Measure the Water Activity**
- 2. See what grows**
- 3. Consumer potential**
- 4. Packaging**
- 5. Product life**
- 6. Challenge test procedure**
- 7. Add the preservative**
- 8. Safety**

# Developing a challenge test

- The same test might not give relevant results for different types of products
- Many products are over preserved
  - You try one level and if it works, you should try it at a lower level
- Clearly atypical cosmetics cannot use classical methods.
  - “Teach to test”

# Types of Products

- **Typical**
  - Water is the external phase (O/W emulsions) or solutions
    - Most PET tests give good results
- **Atypical**
  - All others including W/O emulsions
    - Difficult to test
    - Do they need to be preserved?
    - New guidelines from the PCPC's micro committee



# In General

- Use Combinations
- Must be in the water phase
- Incorporate “active” chelating agents

# Water Activity

- Freidel: The Application of Water Activity to Microbiological Attributes Testing Non-sterile OTC Drugs
- $A_w$  The vapor pressure of the solution @°C divided by the vapor pressure of pure water at the same temperature
- Scale of 0 to 1.00
- **Measured only by instrumentation !!!**
- 0.60 to 0.99 is the range for growth

# Applications of $A_w$

- Prevents growth
- Must have GMP's, HACCP
- Ingredients that lower available water include glycols, salt
- Not for amateurs!

# HACCP

Hazardous

Analysis

Critical

Control

Points

# Requirements for Growth

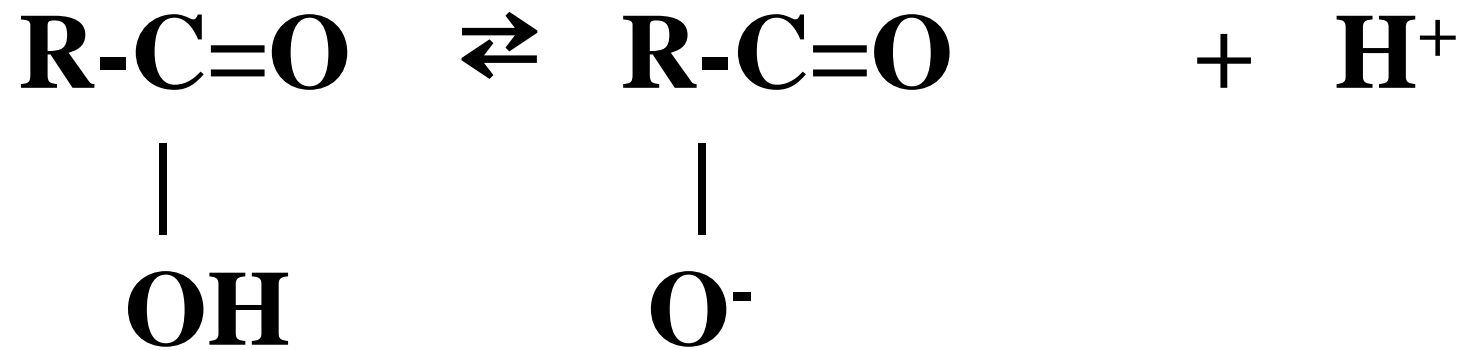
- **Mold:** 0.70 to 0.98
- **Yeast:** 0.88 to 0.91
- **Gram +:** 0.86 to 0.98
- **Gram-:** 0.91 to 0.98

# Frequency of Use of Preservatives 2010

# Frequency of Use of Preservatives 2015

• Methylparaben	13,821
• Phenoxyethanol	13,004 ↑
• Propylparaben	10,615
• Butylparaben	5,081
• Ethylparaben	4,950
• Methylisothiazolinone	4,313 ↑
• Benzyl Alcohol	3,702 ↑
• Caprylyl Glycol	3,677 ↑
• Methylchloroisoithiazolinone	3,507 ↑
• DMDM Hydantoin	2,457

# Acid Chemistry

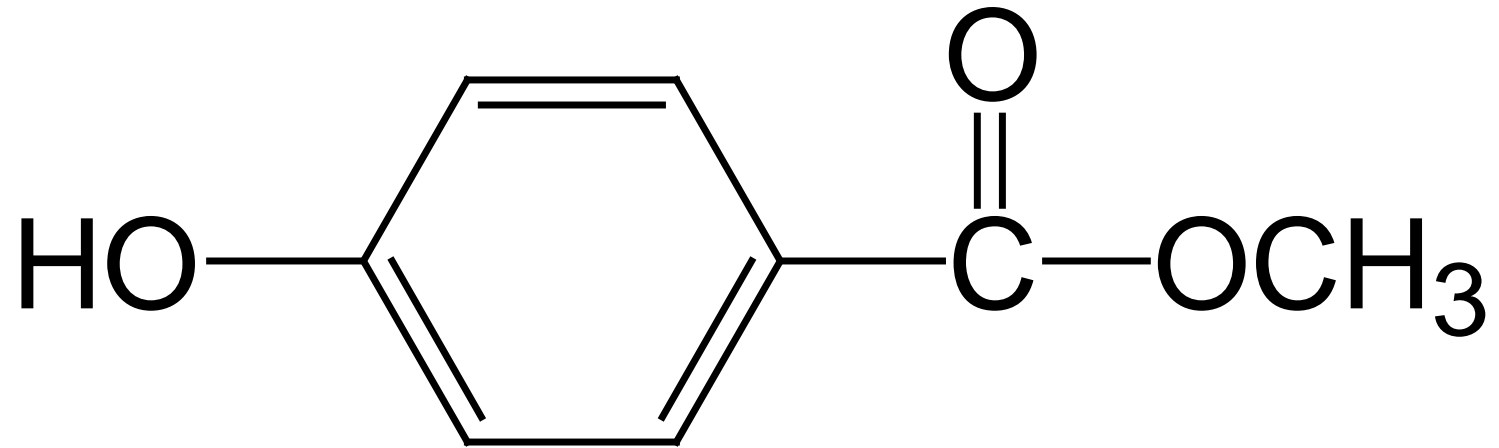


**Active**

**Inactive**



# Methylparaben



# What Does This Mean?

- Salts are not preservatives, only the free acid is
- pH is critical
- Applies to quaternary types also

# Preservatives at Different pH's

pH	3	4	5	6	7
DHA	100	95	65	16	2
Benzoic	94	61	13	1.5	0
Sorbic	98	85	37	5.5	0
Salicylic	48	9	1	0	0
Formic	85	36	5	1	0
Propionic	99	88	43	7	1

# Solubility of Parabens

<b>Ester</b>	<b>25°C</b>	<b>80°C</b>
<b>Methyl</b>	<b>0.25</b>	<b>2.0</b>
<b>Ethyl</b>	<b>0.17</b>	<b>0.86</b>
<b>Propyl</b>	<b>0.05</b>	<b>0.3</b>
<b>Butyl</b>	<b>0.002</b>	<b>0.15</b>

# How to add Parabens

- The wrong way
- Your way in the lab
- The European way
- My way
- The alternative best way

# Paraben Issues

- Japanese paper on reduction of sperm count
- EU papers on endocrine disruptors
- Found in Breast cancer tissues
- EU has limited Propyl and Butyl to 0.19 max. (total). Ban of iso's, Benzyl and Phenyl have been published
  - Least effective

# Parabens

- NGO's/Marketing-You can't use them!
- Scientists-why not? They are the safest and most commonly used preservatives for over 95 years.
- NGO's/Marketing-They are harmful, they are found in breast tumors, and they have estrogenic activity
- Scientists-Nonsense!

The above mentioned studies have resulted in scientific debate that in turn led to popular controversy, largely propagated by mass e-mails and other social media. The controversy has led to some concerns (both over its possible carcinogenicity, as well as estrogenic effect), being expressed over the continued use of parabens as preservatives. The scientific community has found no correlation with cancer and mostly agree that any causation is improbable.



FDA-Although parabens can act similarly to estrogen, they have been shown to have much less estrogenic activity than the body's naturally occurring estrogen. For example, a 1998 study found that the most potent paraben tested in the study, showed from 10,000- to 100,000-fold less activity than naturally occurring estradiol (a form of estrogen).

Paraben-Free has become a common marketing claim

CIR: Safe and many re-reviews

# Paraben Scoreboard

- EU has new restrictions as of 4-9-14
  - Prohibits iso parabens and benzylparaben
- Not to be used in baby wipes
- EWG:

Low hazards score	0-2
Moderate hazards	3-6
High hazards	7-10

# EWG Paraben Scorecard

- Methyl 4
- Ethyl 4
- Propyl 10
- Butyl 7
- Isopropyl 7
- Isobutyl 7
- Acid 3
- Benzyl 2!
- Salts 0!

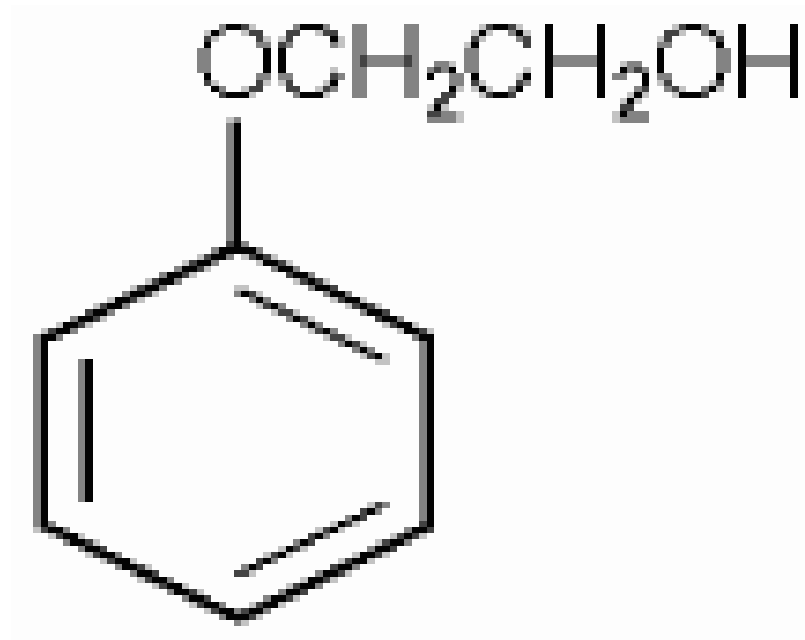
# Latest CIR Findings 2017

- Added the Potassium, Sodium and Calcium salts of Para acid
- Added the above salts of all Paraben esters
- All are safe as used
- None of these are used!

# Aromatic Alcohols

- These alcohols have acidic Hydrogen's and are therefore pH dependent
  - Parabens
  - Phenoxyethanol
  - Benzyl Alcohol

# Phenoxyethanol



# Phenoxyethanol

- This material is produced from 1 mole of EO on phenol.
- It is a weaker acid than parabens.
- Some activity against bacteria, yeast and molds.
- Good solvent for parabens and some other preservatives.
- It has a rose aroma and is used in fragrances.
- Liked the parabens, it is universally permitted.

# Phenoxyethanol

- Trace amounts of phenol, 1,4 –dioxane
- Hated by French as a 1 mole ethoxylate
- EWG: 4
- Often called an irritant, reproductive damage, neurotoxin
- CIR-ok
- EU-reviewed by SCCS in 2017, found it is safe up to 1%
- Japan-ok
- Campaign for Safe Cosmetics-chemical to be avoided



# Other Phenolics

- Benzyl Alcohol. This is most active against Gram positive bacteria. It has some activity against Gram negative bacteria, and yeast, but is weak against mold. It is an EU Fragrance allergen. Subject to oxidation.
- Phenethyl Alcohol. Active against bacteria but weak against fungi.
- Chloroxyleneol. Active against mold, poor water solubility and odor.
- Dichlorobenzyl Alcohol. Strongly anti-fungal, difficult to dissolve.

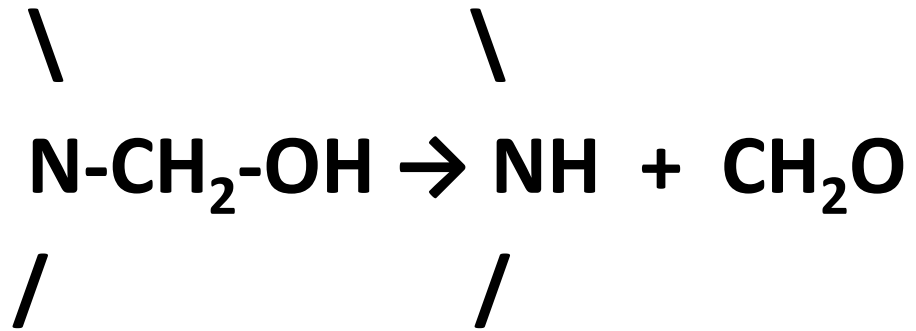
# Benzyl Alcohol

- EWG 5
- EU Fragrance allergen
- Skin anesthetic
- Oxidizes readily
- Weak preservative activity
- “natural”

# Products That React with Acetylacetone

- Hantzsch method
- Reaction of the Nash Reagent
- Forms a color
- Temperature and time dependent

# N-Methylol Groups



- Strength of N to C bond

# Four Common Methods

- Japanese
  - 30 minutes
  - 40°C
- EU
  - 10 minutes
  - 60°C

- CTFA
  - 10 minutes
  - Steam bath ~ 100°C
- L'Oreal
  - 60 minutes
  - 60°C

# Other Methods to Measure “Formaldehyde”

- Chromotropic Acid
- 2,4-Dinitrophenylhydrazine
- Sodium Hydroxide/Hydrogen Peroxide
- All methods are destructive
- What do these results mean?
- EU requires warnings above 500 ppm
  - IARC has moved this to Category 1 CMR
  - May cause this to be prohibited

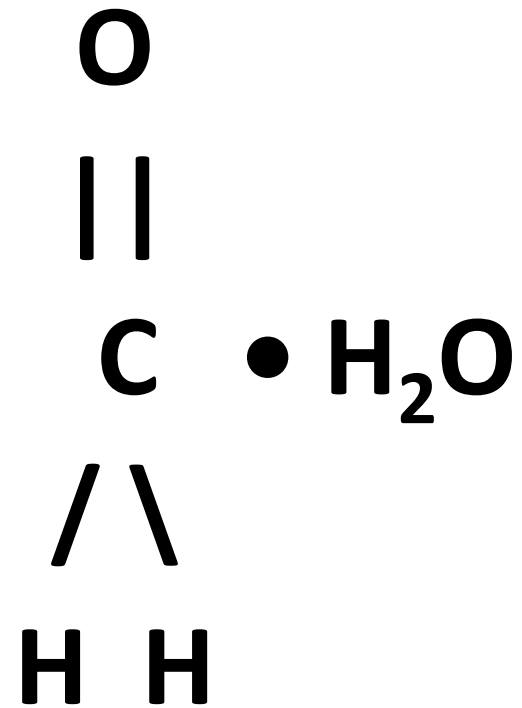
# Preservatives of This Class

- “Formalin”
- Imidazolidinyl Urea
- Quaternium-15
- DMDM Hydantoin



- Bronopol
- Diazolidinyl Urea
- Sodium Hydroxymethylglycinate

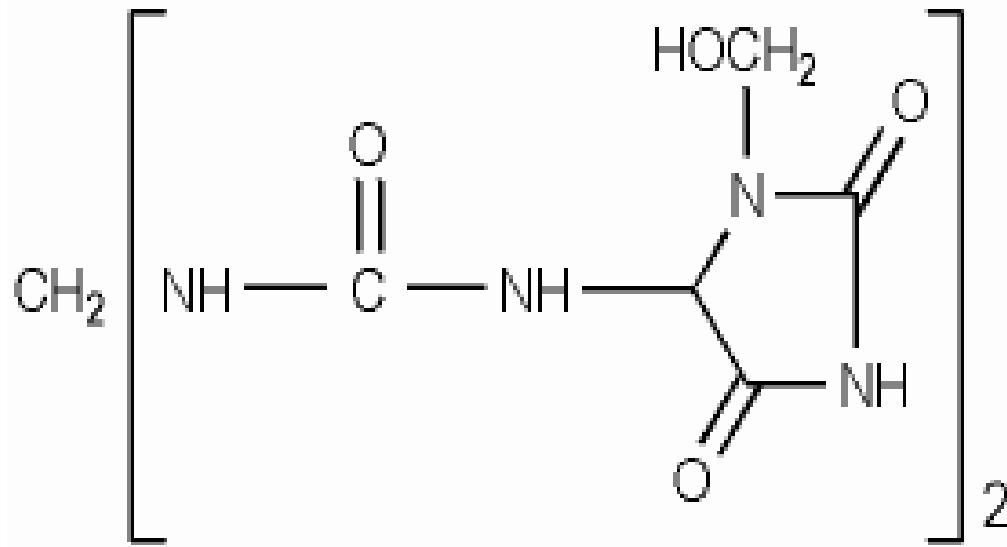
# Formaldehyde (Formalin)



# Methylene Glycol

- Formaldehyde is the correct designation for the anhydrous gas
- This reacts rapidly with water to form methylene glycol (99.94%).
- Formalin is a name for Methylene glycol solutions
- Formaldehyde has never been used in cosmetics

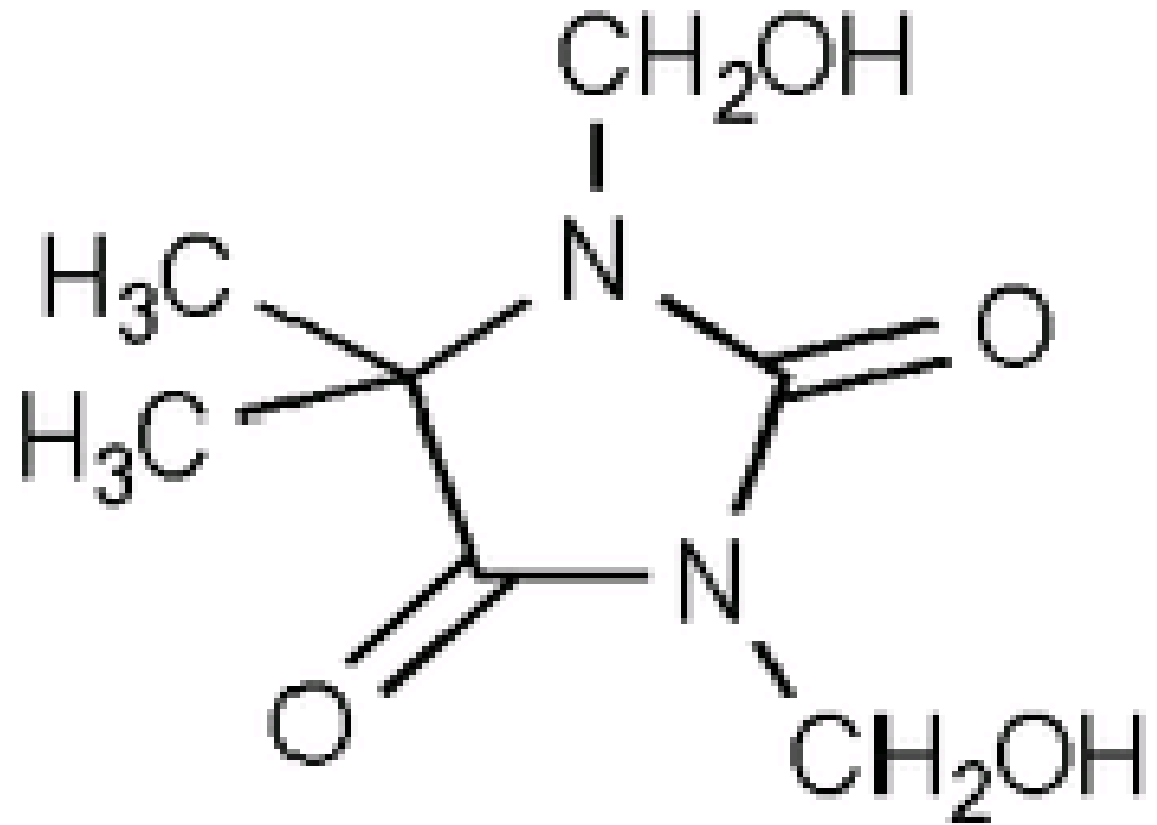
# Imidazolidinyl Urea



# Imidazolidinyl Urea

- EWG 6
- Formaldehyde releaser
- Restricted to rinse-off only in Japan
- Issues in Minnesota for products for children

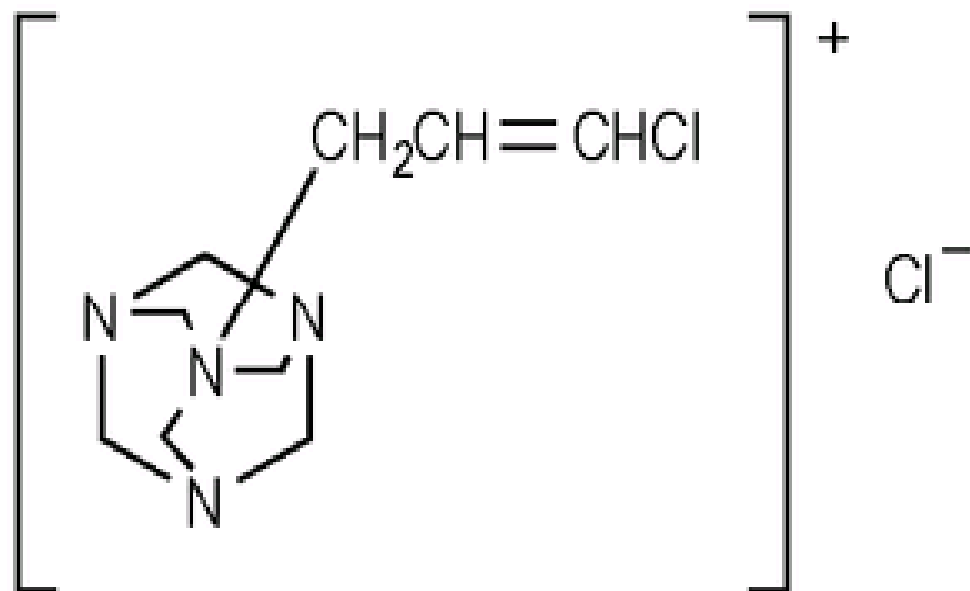
# DMDM Hydantoin



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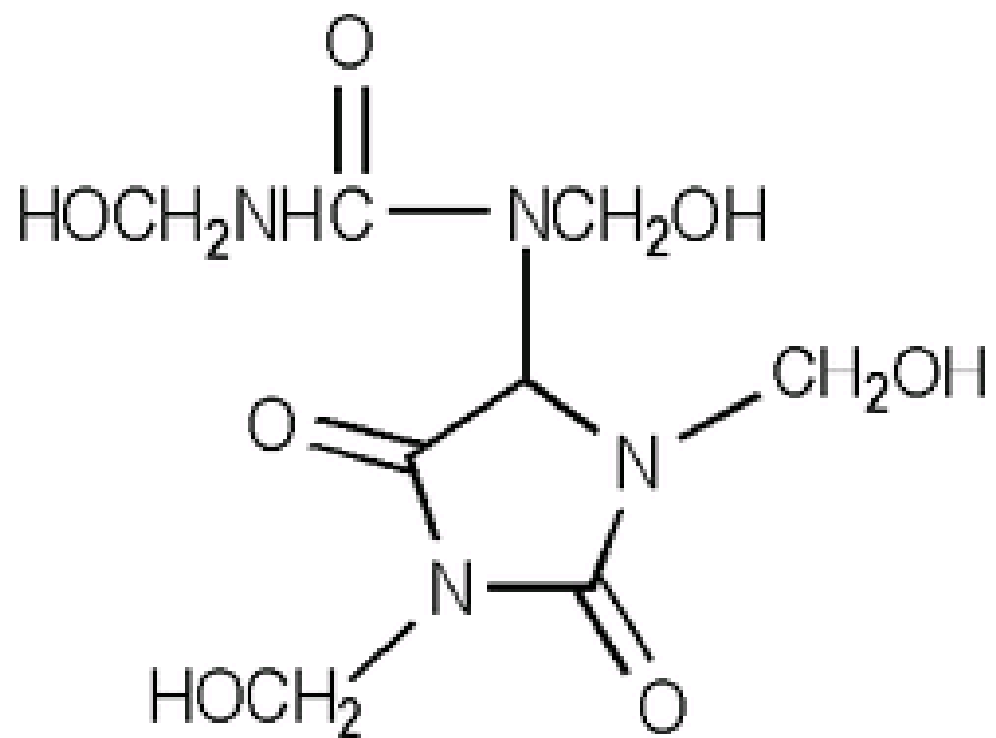
- EWG 7
- Formaldehyde releaser
- Restricted to rinse-off only in Japan (powder)
- Issues in Minnesota for products for children

# Quaternium-15

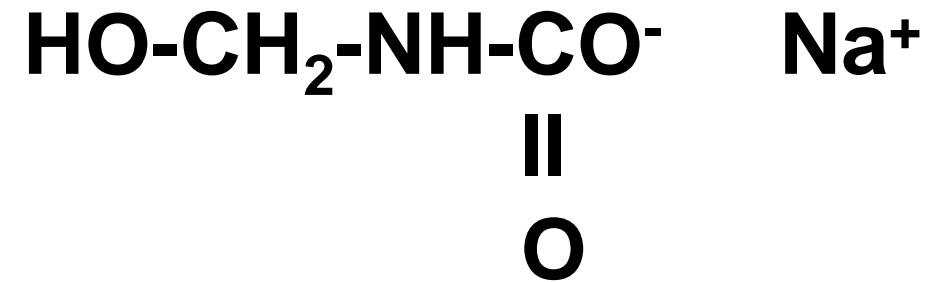




# Diazolidinyl Urea



# Sodium Hydroxymethyl Glycinate



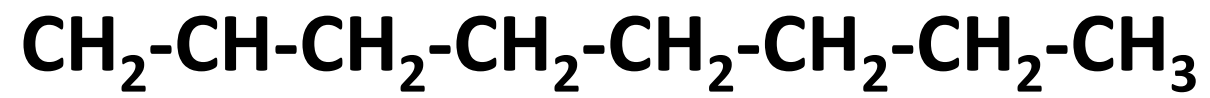
# EWG Scorecard

- **Quaternium-15** **8**
- **Diazolidinyl Urea** **6**
- **Sodium Hydroxymethyl Glycinate** **6**

# 1,2 Diols

- Pentylene glycol
  - EWG 0
  - Allergic reactions are known
- Caprylyl glycol
  - EWG 0
  - Allergic reactions are becoming more common
- 1,2 Hexanediol
  - EWG 0
- All are tainted by association with glycol (ethylene glycol)
- **None are approved as preservatives anywhere!**
- Limited safety data!

# Caprylyl glycol



# Formulation Issues

- Acts as an emulsifier
- Order of addition is critical
- Does not function well in surfactant systems
- Water solubility is a problem

# Combinations

- Why?
  - Broader Activity
  - Ease of Incorporation
  - Dilution of Actives

# Current Preservatives Being Attacked

- Triclosan (not used as a preservative!)
- Parabens
- Glycols
- “Formaldehyde” releasers
- Isothiazolinones
- Phenoxyethanol
- Benzoic Acid



# Triclosan

- It is a pesticide!
  - **All preservatives approved by the EPA are classified as pesticides**
- Contains chloroform
  - None found
- Contains dioxin
  - Must meet USP specifications. Very small trace amounts are permitted (ppb)
- It is an endocrine disrupter
  - No evidence
- Causes antibiotic resistance
  - Original paper claiming this has never been duplicated

# What the FDA Says About Parabens

- Parabens are acknowledged to be an endocrine disrupter that can act similarly to estrogen. However, FDA notes that studies have shown parabens have much less estrogenic activity than estrogen naturally occurring in the human body. Because parabens are used in such low levels in cosmetics, researchers have concluded that it is “implausible that parabens could increase the risk associated with exposure to estrogenic chemicals.”
- The most common study cited by opponents of parabens shows that parabens were detected in breast tumors. The authors of the study note that parabens can act like estrogen and that estrogen has an impact on the development of breast cancer. However, the FDA has noted the study’s limitations, stating: “For example, the study did not show that parabens cause cancer, or that they are harmful in any way, and the study did not look at possible paraben levels in normal tissue.”

# Glycols

- Rapidly gaining in popularity, especially the C-8 1,2 diol (INCI Caprylyl Glycol)
- Denounced because of toxicity of ethylene glycol and diethylene glycol
- Guilt by association

# “Formaldehyde” releasers

- Formaldehyde is a very popular buzz word to scare consumers.
- An example is the report-“The Toxic Tub”
  - The manufacturer of Quaternium-15 no longer supports this for most cosmetic uses
- The safety of these type preservatives has been thoroughly studied and found to be safe.

# Isothiazolinones

- Pesticides
- Neurotoxins
- Allergens
- Known human immune system toxicant
- Found safe at cosmetic use levels and restricted applications
  - Using MIT at its EU/Japan maximum levels has resulted in increase allergy reports (contact allergen of the year!) and new EU restrictions.
  - CIR maintained its assessment as safe, but added: to be formulated to be non-sensitizing.
  - EU & Canada have banned the use of methylisothiazolinone and the MCI/MI mixture from leave on products

# Phenoxyethanol

- Originally used as a paint stripper solvent. Very low purity and safety issues.
- It is a known sensitizer
- It can be absorbed by the skin and is teratogenic
- Like all ethoxylates, it can contain trace levels of 1,4 dioxane
- NGO's love to confuse the public with 1,4 dioxane and dioxin (Agent Orange)
- We only use the high purity material.

# Benzoic Acid

- Natural benzoic acid is safe.
- Synthetic is not!
- Benzoic acid contains benzene.
- Benzoic acid reacts with ascorbic acid to form benzene
  - Even the FDA sort of believes this!
  - This has been perverted to say benzoic acid reacts with citric acid to form benzene!

# How?

Benzoic acid is made from the oxidation of toluene or the reaction of benzene with carbon monoxide.

How can benzoic acid react with ascorbic acid or citric acid to form benzene?



# Marketing Restraints on Preservatives

- Does marketing prevent you from using certain preservatives for market appeal?
  - Parabens
  - Chlorinated or iodine chemicals
  - Contains Ethylene oxide
  - Formaldehyde
  - Isothazolinones
  - Glycols
  - Alcohols
  - Acids

**Why?**

# The Issue

- NGO's have been attacking chemicals for years and have been focusing on preservatives.
- Their goal is always the same:

# MONEY

- They achieve this by scaring people
- They have two willing accomplices
  - The media
  - The marketers of cosmetics

# The Major Player

- The Environmental Working Group (EWG)

“The mission of the Environmental Working Group (EWG) is to use the power of public information to protect public health and the environment.”

- Go to their website and the first thing you see is a request for money!

# Follow the Money

- Over ½ of the money raised goes to the employees and directors as salary and bonuses
- They raise money:  
**see CORE: The Center for Organizational Research and Education is a 501(c)(3) nonprofit dedicated to research and education about a wide variety of activist groups, exposing their funding, agendas, and tactics.**

They have established the Center for Accountability in Science

The EWG has a history of passing shady “science” off as solid facts. Their main talent isn’t research, it’s duping reporters into credulously transcribing their “findings.” A nonprofit organization that has learned how to turn **public panic** into a stream of hefty donations, the Environmental Working Group has no problem ginning up outrage that causes families needless worry and does incalculable damage to honest industries.

# **Their True Philosophy**

Don't confuse me with facts,  
my mind is made up.



In reality, the Environmental Working Group is a cauldron where many of the worst pseudoscience smear campaigns are cooked up. They prey on the public's distrust of polysyllabic scientific jargon -- and reporters' ignorance of the same -- to make it sound as if everyday items with complicated names are, in fact, deadly dangerous.

The EWG's game plan is simple. It releases "scientific" analyses designed to make the public (especially parents) worry about extremely tiny amounts of "toxins" in everyday items. It throws around scary phrases like "cancer risk" and "nervous system toxicity" that is catnip for environmental reporters, many of whom uncritically pass along the EWG reports without scrutiny or fact-checking. If the EWG had its way, America would turn its back on the scientific advances that make our crops more productive, prevent cancer, and keep our foods fresh and safe.

# Followers

- Many other NGO's follow their lead.
- Skin Deep is actually part of the EWG
- The Campaign For Safe Cosmetics shares the same officers
- Many cited support groups consist of 1 or 2 people with a web site.
- They encourage cosmetic companies to join them.
- DO YOU?

# Results

- Their scientifically discredited campaign against the use of mercury preservatives in vaccines, has lead to many parents refusing to inoculate their children out of fear.
- This has resulted in increase cases of almost extinct childhood diseases.
- California just passed legislation that requires vaccinations of children to attend public schools.

# Their Basic Philosophy

- If it is natural, it is safe
- If it is a chemical, it is toxic
- Industry doesn't care about safety, only money
- Government is paid off by industry
  - We call this user fees!
  
- If the first attack doesn't work, change the attack
- If you repeat it often enough, the public believes it is true

# Who Encourages This Pseudo Science?

- **The marketers of Food, Drug and Cosmetic products!**
- They are quick to claim .....”Free” to sell one more bottle.
- An example-Colgate has a new liquid dish detergent claiming triclosan free. Yet Total<sup>®</sup> toothpaste (their largest selling product!) has triclosan as the active ingredient!

# The Latest Disaster

- The “organic” and “natural” market subscribes to the theory that all preservatives are bad. The only ones they permit are weak and usually ineffective. **Further they cannot be made from petrochemicals.**
- But now, we find massive contaminations of their products usually coming from poor GMP’s, but especially coming from spores in their raw materials.
- What do you expect when these are grown with “natural” fertilizers?

# What Can You Do if You Can't Use Preservatives That Work?

- Manufacturer under strictly enforced cGMP's. (spend the big bucks!)
- Establish and use HACCP to find where contamination is taking place and eliminate it. (spend the bucks)
  - Hire a good consultant (this is a paid political announcement)
- Package your products so consumers cannot contaminate them. (spend big bucks)
- Insist that your company stop the self destructive behavior of claiming ...."Free" (fire your marketeering department!)
- Do not use ingredients from suppliers who sell by being negative!
- If you are brave enough, tell marketing the costs of not using good, safe preservatives.



# New Preservatives

- In 2008, I presented a talk on how every preservative that we use is under attack.
  - Even though the safety record has been reviewed time and again and they have been found to be safe.
- Will there be new preservatives?
  - NO!

# What Does Marketing Want?

- Natural
  - Only thing natural is earth, wind, fire and rain
- 100% Safe
  - There is no 100% safety-the dose is what is important.
- Works in all products.
- Has never been tested on animals.
- Protects against all possible contamination in your plant, ingredients and by consumers.
- Be allowed world-wide
  - There are 206 recognized countries in the world. Could you narrow this down?
- Be cheap!

# Why Is this Impossible?

- In the 1960's a new preservative was introduced with about \$2,000 of safety testing-LD50, Eye irritation-rabbits, Skin irritation-guinea pigs
- In the 80's the first preservative cocktail was introduced, based on existing preservatives and over \$100,000 of safety testing was performed.

# The Last New Preservative

- Took over 5 years to obtain approvals in the EU, Japan, China.
- Costs were in the 7-8 figure range.
  - Now it will be prohibited next year!
- Today a new chemical, besides the safety testing for cosmetic use, approvals by countries that require pre-approval for preservatives, we have environmental listings such as REACH, DSL, IESCS, NICNAS, etc.
- There will be no new preservative!
  - Our market is just not big enough.
  - The demand for cheap is impossible to meet.
  - Anything found in nature doesn't work and has major issues with what to do with all the by-products.
  - Someone will always attack it.
  - **If it sounds too good to be true, it probably isn't!**

# The Contest

- In late 2016, Green Chemistry and Symrise created the Challenge!
- Deadline was 9/1/17
- New preservative or “booster”
- Prize \$175,000
- 48 entries

# The Future

- We continue to see new non-preservative preservatives offered. (It can't be a preservative-it is not on the approved EU list, so it must be a ..... Which makes our product self-preserving.)
- We continue to see “natural” extracts which function as preservatives, just like dietary supplements work as real drugs.
- **Caveat Emptor!**

# What Can Be Done?

- Support a strong FDA public relations efforts on the safety of cosmetics, the safety of cosmetic ingredients including preservatives, the excellent safety reviews by the impartial CIR, and that the FDA has the authority and uses its authority to ensure that cosmetics are safe.
- History supports the safety of cosmetics and preservatives.  
or
- Support more regulations in the US that requires the FDA to pre-approve all ingredients and all cosmetics!

# The Feinstein Bill

## S. 1014

- Would require the FDA to do a complete safety review of at least 5 cosmetic ingredients a year.
- Priority list:
  - Diazolidinyl Urea
  - Lead Acetate
  - Methylene Glycol/Formaldehyde
  - Propylparaben
  - Quaternium-15

The “bad” guys are winning!



# The Latest Issue

- In February the FDA issued new inspectors guidelines
- <http://www.fda.gov/downloads/Cosmetics/GuidanceRegulation/GuidanceDocuments/UCM208412.pdf>

# Cosmetic Inspection Guidelines 2016

FDA is concerned that cosmetic products that make a statement in labeling that the product is “green”, “natural”, “no parabens” and “no preservatives” may not be safe for consumers without appropriate safety testing. **Companies and products that make such label statements should be given priority over traditionally manufactured cosmetics during inspection and sampling.**

# Inspectors are to

Collect samples of eye area cosmetics, tattoo inks or skin care preparations and lotions for microbiological analysis when:

- 1. adequate challenge test documentation cannot be produced**
- 2. the adequacy of preservation is in doubt**
- 3. or non-traditional preservative systems are used.**

# FDA's Concerns

Another change that the cosmetics industry is **facing is consumer distaste for traditional preservatives**. As an example, parabens, which are one of the most effective classes of preservatives, have been suspected of causing adverse effects to the endocrine system. In the European Union parabens are being phased out of all cosmetics because of this concern. As a result manufacturers are applying non-traditional preservative systems in order to assure the microbial safety of their products.

# Instructions

Since resistance to microbial contamination is especially important in the case of eye area products (especially those that are water-based), tattoo ink, skin lotions and no-alcohol mouthwash, collect samples of recently produced and retained products

- 1. when the manufacturer is unable to produce challenge test documentation or**
2. the adequacy of preservation is otherwise in doubt or
3. non-traditional preservative systems are used.

# Preservative Compounds Commonly Used in Cosmetics

- Parabens (methyl, ethyl, propyl, and butyl)
- Quaternium 15
- Diazolidinyl urea
- Imidazolidinyl urea
- DMDM Hydantoin
- 2-Bromo-2-nitropropane-1,3-diol
- Sodium hydroxyglycinate
- Phenoxyethanol
- Sorbic acid / Potassium sorbate
- Methylisothiazolinone
- Methylchloroisothiazoline
- Sodium benzoate
- Caprylyl glycol
- Sodium dehydroacetate
- Formaldehyde

# Non-Traditional Preservatives

Non-traditional preservatives are typically extracts of botanicals, organic acids, alcohols and glycerols. Fermentation products are also used as preservatives. The presence of these types of chemicals in a cosmetic, in the absence of traditional chemicals, indicates they may be used as part of a preservative system. This list is a small sample.

- Glyceryl caprylate
- Levulinic acid
- p-anisic acid
- Eucalyptus globulus
- Glycyrrhiza Glabra (Licorice) Root Extract
- Salvia officinalis
- Citrus grandis (organic grapefruit) extract
- Arnica montana (organic arnica) extract
- Boraxitrus seed extracts
- Leuconostoc/Radish Root Ferment Filtrate
- Goldseal (Hydrastis canadensis root extract)
- Citrus Medica Limonum (Lemon) Peel Extract
- Caprylhydroxamic acid



# What Should I Do?

## **1. Run water activity**

1. It is cheap, quick and tells us so much
2. Stop worrying about yeast if yeast will not grow!

## **2. Know your packaging that is to be used**

1. This will give you some idea of consumer exposure and possible contamination, also filling issues.
2. Compatibility with preservatives

# Preservative Selection

1. What is your pH? Is It flexible?
2. What is the chemistry of your preservative?
3. Is it simple and easy to analyze?
4. Is it complex and difficult to analyze?
  1. How will you know if each batch is the same?
  2. How will you know if it is working the same?
  3. Is order of addition/temperature critical?

# Critical Comments

- If you want “organic” certification, make sure it allows synthetic made chemicals that are found in nature.
- Be aware that claiming “natural” when it is made from “unnatural” sources is deceptive advertising and can result in large fines/payoffs/lawsuits. Be sure marketing understands this.
- Know the chemistry of what is offered to you and if you cannot understand the origins, be sure the vendor will indemnify you.

# When All Else Fails

- You must have HACCP in place and be followed.
- You must strictly adhere to tough cGMP's to prevent contamination.
- You must allow sufficient time to test many different systems. What worked in a formula may not work in the same formulation with a different fragrance or color.
- Never assume anything-test!
- Finally-when all else fails-try unit dose packaging

# Questions?

David C. Steinberg, FRAPS  
Steinberg & Associates, Inc.

609-799-1575 phone

609-799-5271 fax

[david@steinbergandassociates.com](mailto:david@steinbergandassociates.com)

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