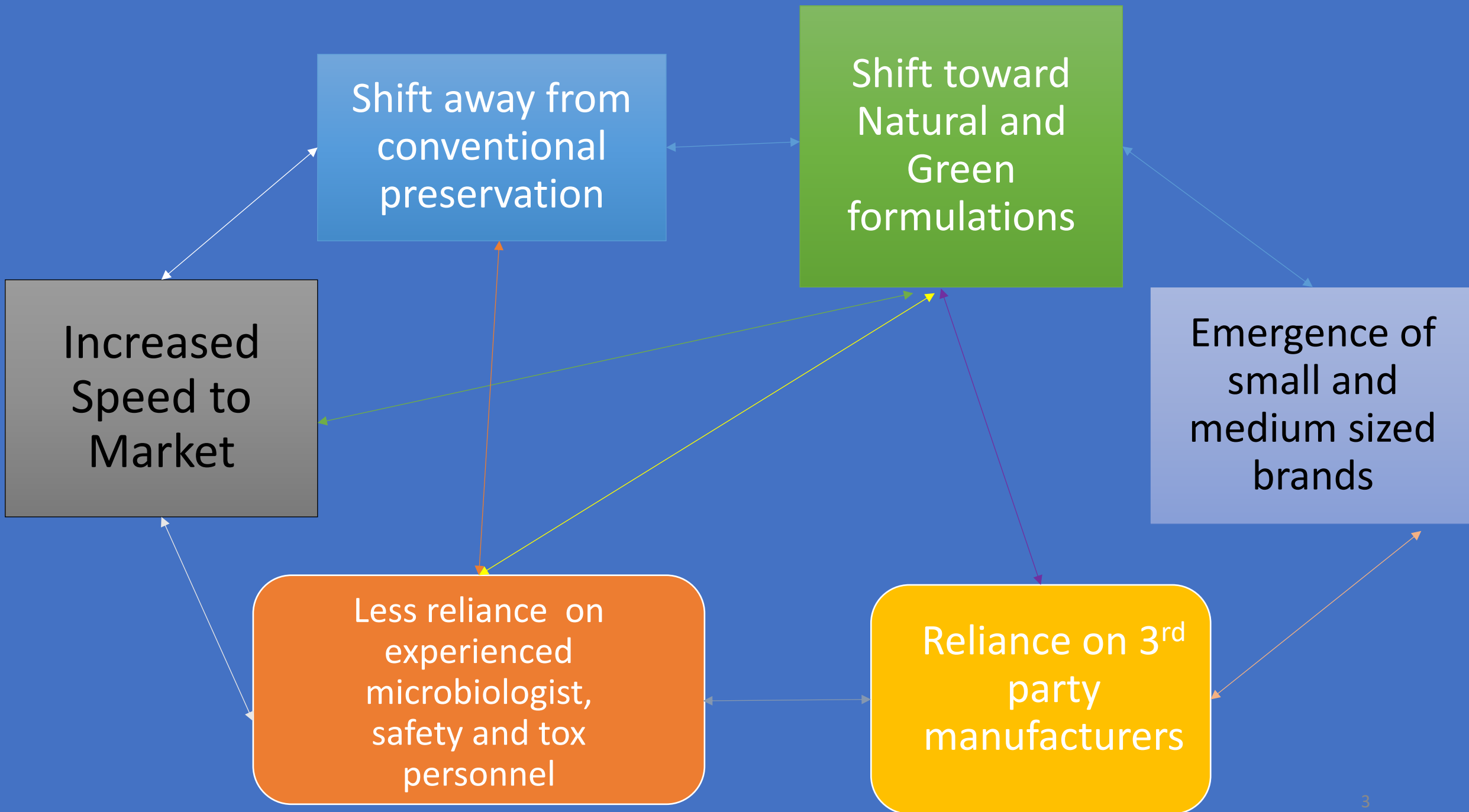


The State of Preservation and Cosmetic Microbiology Today

Steven F. Schnittger
Estee Lauder Companies

Not a Good State of Affairs

- **Constant Pressure on the Use of Conventional Preservative Systems**
- **Consumer and Marketing Pressure to move toward more Natural, Greener and Cleaner Formulations**
- **Increased Pressure to get products out into the market place in a shorter period of time**
- **Work with smaller and middle – sized brands with fewer experienced chemists, microbiologists, and safety professionals which requires more hand holding by us**
- **More reliance on Third Party Manufacturers for development and manufacturing**
- **Introduction of New Innovative Packaging which plays a role in Increased Risk**



Inter-connection

- Companies are moving away from conventionals because consumers want greener formulas
- There is an emergence of small and midsize brands which are driving the market place and using TPM's to manufacture their products
- Smaller brands are using the USP challenge test criteria because of speed to market and because they are relying on feedback from science professionals that may not have the long term experience in product preservation and safety

Mission Statement

- Every cosmetic manufacturer has a dual responsibility relative to the quality of their products:
 - Ensure that the product, as purchased, is free from the number and types of microorganisms that could affect product quality and consumer health
 - Ensure that microorganisms introduced during normal use will not adversely affect the quality and safety of the product throughout its life of that product.

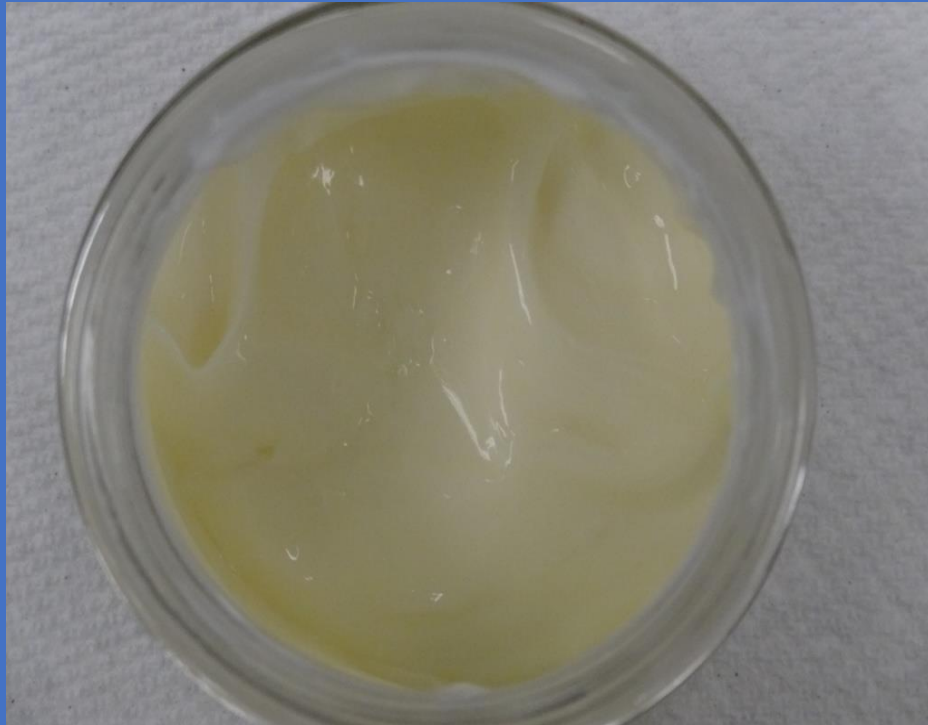


We are
responsible
for both mfg.
and
consumer use

Preservation and Product Protection

- *All aqueous based products require to be preserved or have some form of product protection to minimize the risk of microbial contamination and ensure product quality and stability.*

Adequate Preservation



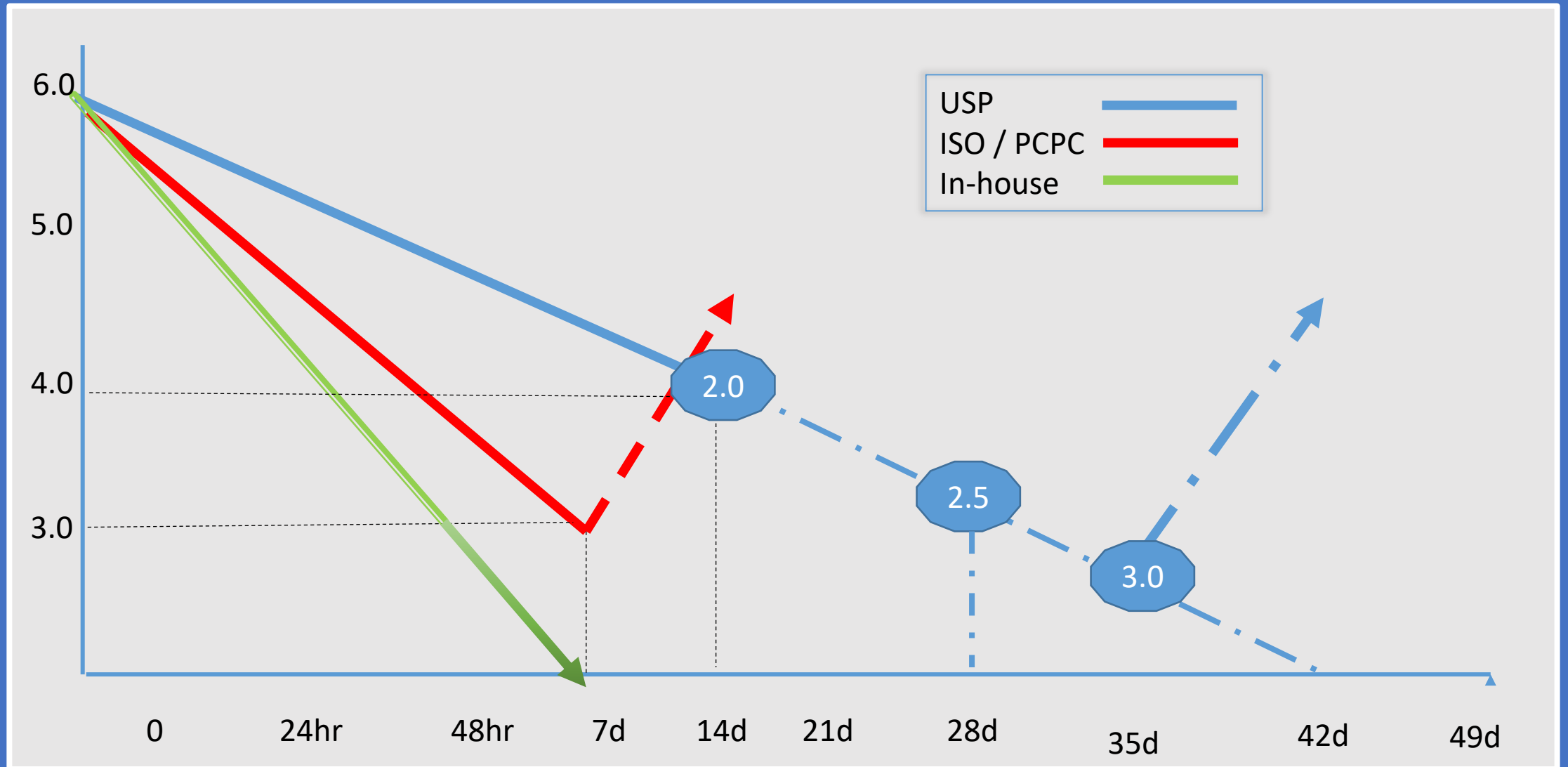
Adequately Preserved



Inadequately Preserved

Challenge Test Criteria

Challenge Test Criteria Potential Rebound Effect



Potential Risk

- If you are preserving to meet the USP you may be under preserving which may lead to long term instability and contamination at later time points
- It may give you a false sense of security that your product is adequately preserved
- The formula may not be preserved well enough to protect against low levels of contamination

Adequate Preservation



Adequately Preserved



Inadequately Preserved

What are your options?

- Use either the ISO or PCPC or in-house method whose criteria is stricter than USP
- Perform a re-challenge to ensure long term efficacy
- Make sure you challenge samples at each step of development

Make sure you have a complete profile of the formulation during scale up

❖ *Lab, pilot, production, filled container and stability*

- Understand the risk that is involved in using the product in its final package and evaluate the risk

Eye area versus body product

- Make sure that you have a form of stability in the final package or similar container type again to determine risk

Clinical Evaluation in Final Package

Challenge Test Profile

[illegible]

The Art of Preservation and Product Protection

Product Protection - A Multi-faceted Approach

- Protection can be delivered solely based on chemicals *whose only function is preservation*.
- Protection can also be delivered through multifunctional ingredients whose primary attributes may be some function other than preservation, but does contribute to the preservative efficacy of the formula

Physiochemical Factors

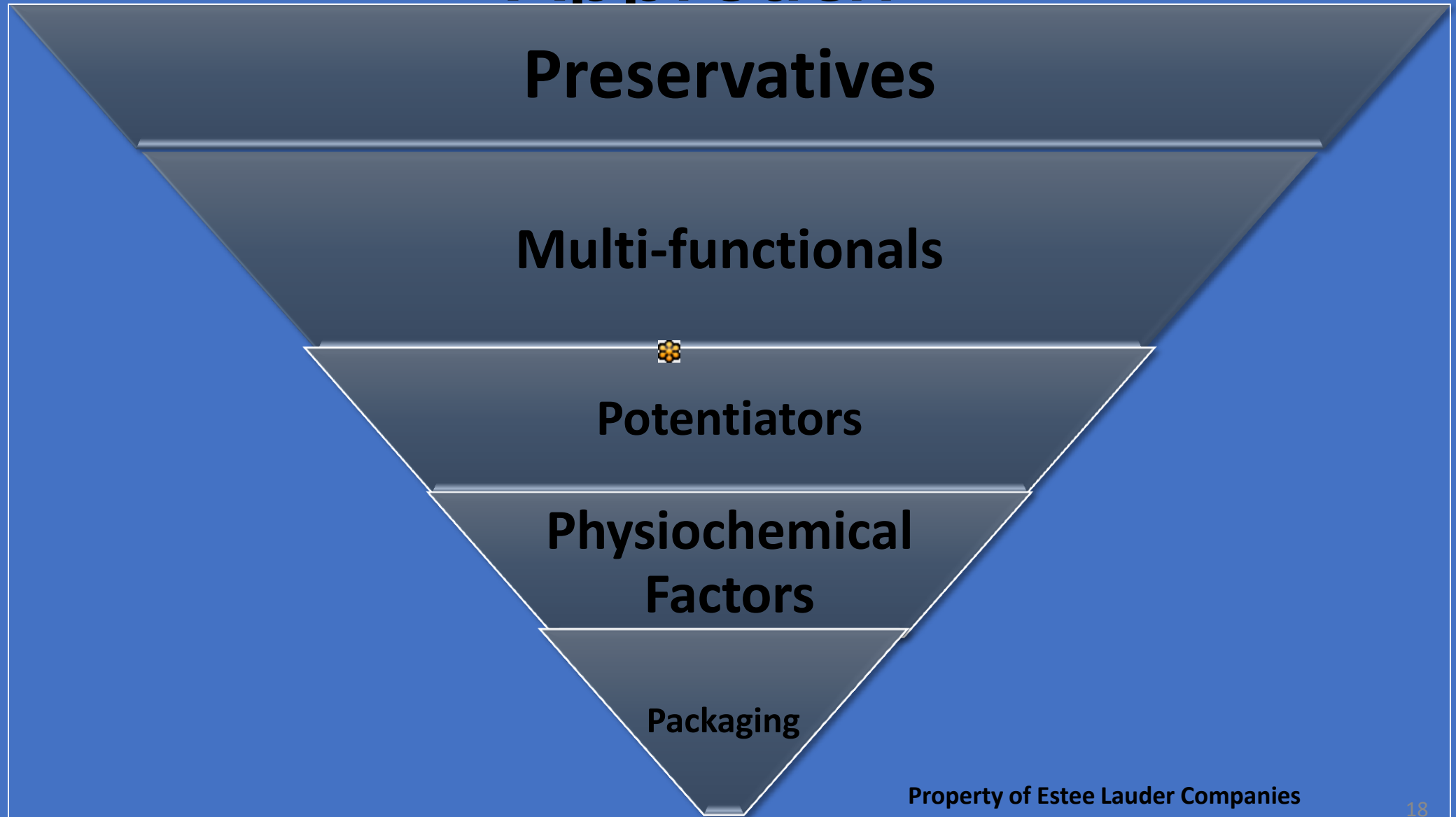
- Product protection can also come from physiochemical properties such as pH, reduced water activity, or mfg. / fill temperatures which creates an environment which is recognized as low risk to microbial growth (ISO 29621)
- *These properties play a minor role in aqueous based products, but may play a major role in protecting anhydrous products.*

Risk Assessment and the Role of Packaging

- The final method of protection is through the use of packaging which could help minimize the ability of the consumer or the environment to contaminate the product
- The combination of packaging and risk assessment help to determine product risk and testing requirements.

Property of Estee Lauder Companies

Production Protection: A Holistic Approach



Preservatives



Conventionals

Parabens · Formaldehyde Donors ·
Isothizolones ·
Halogens · Alcohols

Multifunctionals

Glycols · Glycerin derivatives · Alcohols · Chelators ·
Anti-oxidants

Multi-Functional Ingredients

- Industry has moved to using Multi-Functional Ingredients to help potentiate the preservative efficacy of their formulations and fill the gap in the loss of conventionals
- When used in combination with conventional systems data shows synergy preservative efficacy with improved efficacy so there clearly are benefits.

But there are also risks:

- Many companies are using these ingredients for their claims and competitive advantage

What are the Risks?

- Companies are making preservative free claims
- Making claims that are not aligned with Annex V
- Many non-conventionals are pH or formula dependent and they will lose efficacy if formula is not stable over time
- Long term efficacy of many non-conventionals has not been fully established
- Combining non-conventionals with a minimal P.E.T criteria could result in a false sense of security

Regulatory Status of Traditional Preservatives

Europe – EU 1223/2009, Annex V – List of Preservative Allowed in Cosmetic Products

- Defines Maximum Allowed concentrations, Limitations and Requirements

Japan – MHW Positive Preservative List

- Defines those preservatives that can be used in all products
- Defines those preservatives that are restricted for certain applications

If an ingredient is being used as a preservative or claims to have preservative efficacy and is not on these lists then you cannot use that ingredient as a preservative

The Making of the First Completely Preservative-Free Skincare Product in the World!

- The Preservative-free Skin Care System is a unique, water-based skin care component offering a natural, fragrance-free product line with ingredients such as Emperor's Green Tea.
- But what really sets this exclusive skin care system apart is that it contains no preservatives.
- Both synthetic and natural preservatives have been shown to have negative effects on the skin.
- The basis for the revolutionary skincare was the utilization of bacteriostatic Tensa water where bacteria simply can not grow – this is the reason why no preservatives are required.

Eye Cream

Water, squalane, glycerin, dimer dilinoleyl dimer dilinoleate, stearic acid, glyceryl stearate, beeswax, polysorbate 60, phytosteryl/isostearyl/cetyl/stearyl/beheryl dimer dilinoleate, **pentylene glycol**, peg-10 stearate, behenyl alcohol, octyldodecyl pCA, butylene glycol, dipalmitoyl hydroxyproline, glyceryl stearate Se, tocopheryl acetate, dimethicone, arginine, trehalose, hesperidin methyl chalcone, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, pimpinella anisum (anise) fruit extract, dipeptide-2, palmitoyl tetrapeptide-7, yeast extract, iris florentina root extract, artemia extract, hericium erinaceum extract, camellia sinensis leaf extract, kjellmaniella gyrata extract, **caprylyl glycol**, steareth-20, **ethylhexylglycerin**, aminoethanesulfinic acid, etidronic acid.

Types of Alternative Preservative Systems

- Glycols and their blends
- Glycerin Esters and their blends
- Essential Oils
- Plant and Botanical Extracts
- Peptides
- Organic Acids
- Phospholipids

Alternative Preservatives with Alternative Functions

Multi-functional Activities include:

- Anti-oxidant
- Chelator
- Fragrance item
- Humectant
- Moisturizer
- Skin and Hair Conditioner

Glycols – Multi-functional, Potentiators, Humectants

- **Propylene, Butylene Glycol (3.0 – 6.0%)**
 - improves solubility
 - reduces oil/water partitioning
 - improves stability
 - **Used as a Preservative Potentiator**
- **Hexylene, Pentylene Glycol (1.0 - 2.0%)**
 - **Used as a Multifunctional with Antimicrobial Properties**
 - Moisturizer
 - Formulation stabilizer
- **Caprylyl Glycol (0.5 - 1.0%)**
 - **Used as a Multifunctional with Antimicrobial Properties**
 - Improves skin hydration

Capryly Glycol

1,2 Octanediol

- Soluble in both water and cosmetic esters
- Has antimicrobial, moisturizing and humectancy activities
- Can also be used as solubilizer or delivery system
- Shown to have synergy with many conventional preservative system
- **Has broad spectrum activity at all pH ranges**
 - **Limited fungal activity**
 - **Used in combination with organic acids**

Caprylyl Glycol

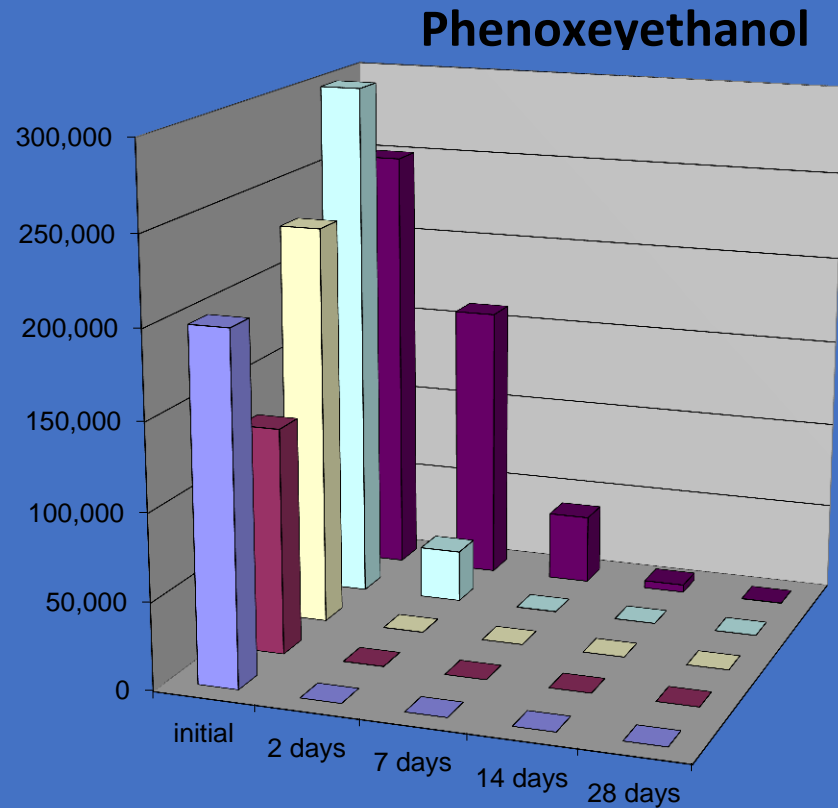
- Synergistic activity comes from its ability to help in penetration through the cell wall.
- Anti-microbial activity comes from its ability to disrupt the cell membrane
- **Main benefit is that it stays at the water / oil interface where preservation is needed the most.**

Caprylyl Glycol

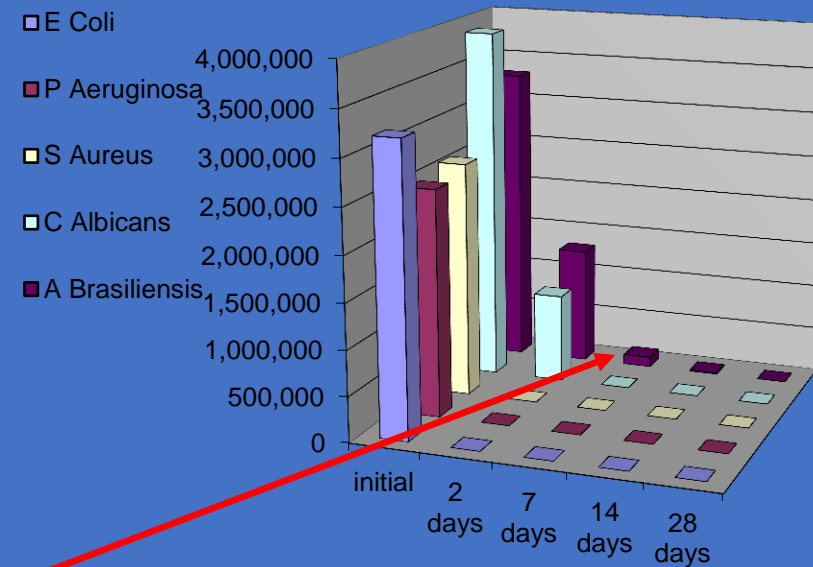
- Used in combination with many other preservatives to help boost their activity:
 - **Phenoxyethanol**
 - **Kathon CG**
 - **Sorbic Acid**
 - **IPBC**
 - **Chloroxyleneol**

CAPRYLYL GLYCOL

Synergy with Phenoxyethanol

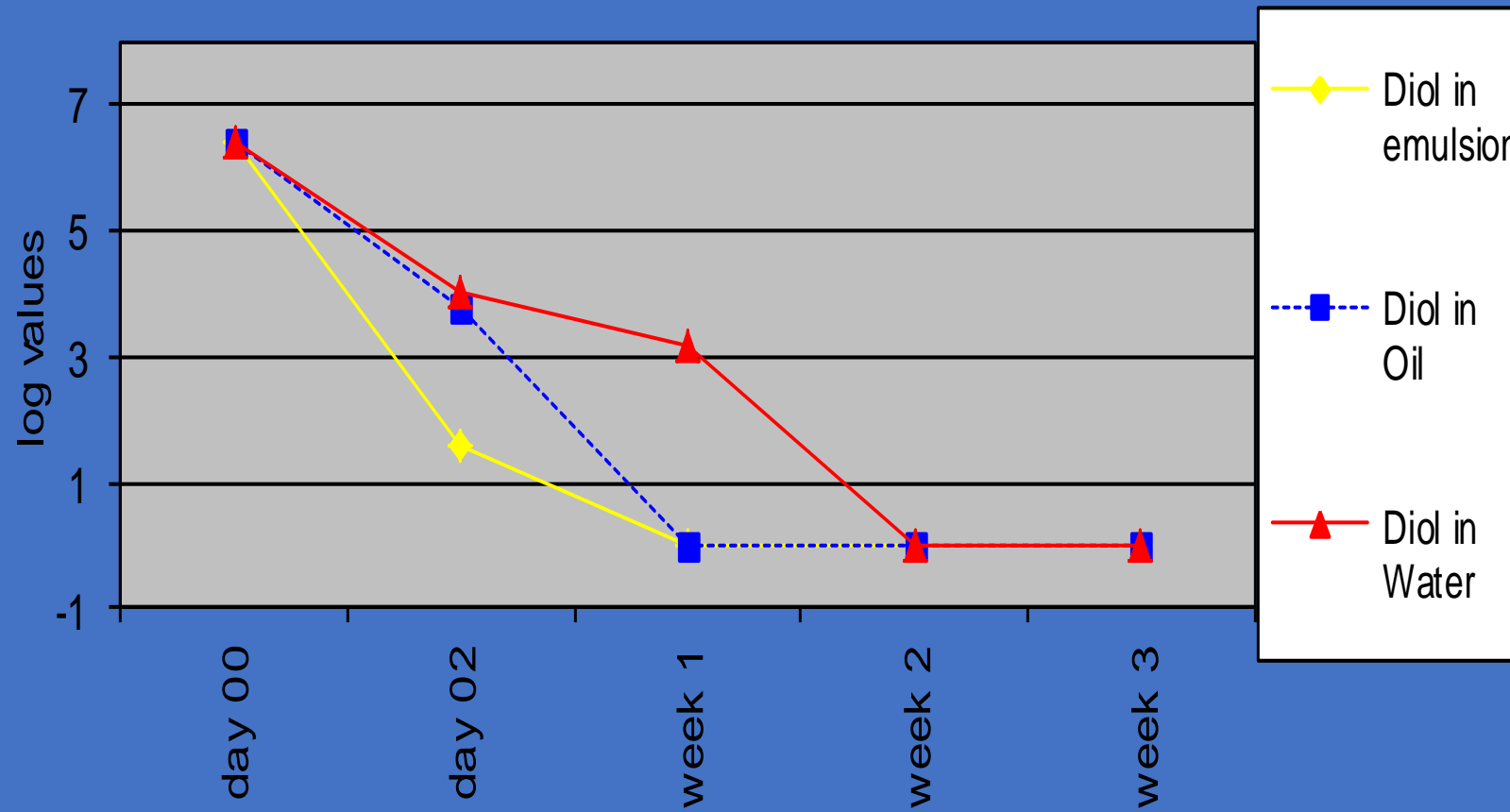


Phenoxyethanol + Caprylyl Glycol



Caprylyl glycol works well with many preservatives/boosters to provide quicker kill

Efficacy of Caprylyl Glycol; Effect on Order of Addition



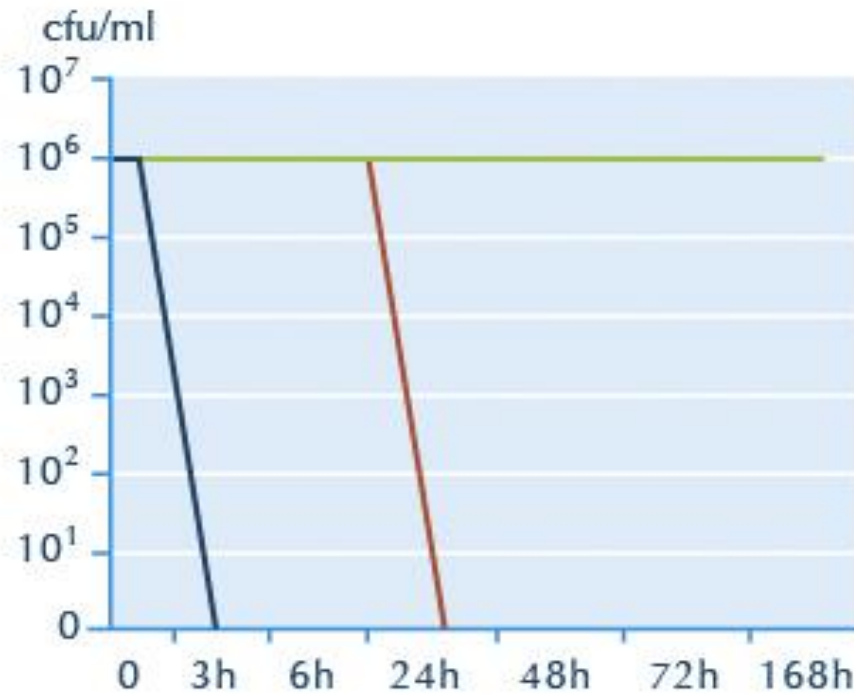
Ethyl-hexyl-glycerin




- **Acts as both a preservative and preservative booster**
 - **Shown to have Synergy with Phenoxyethanol, Isothizolone and Methyl Paraben**
- **Use Concentration 0.1 – 0.5%**
- **pH range 2-12**
- **Multifunctional ingredient activity includes: Deodorizing agent, Humectant and Emollient**

Ethyl – Hexyl Glycerin

Improved efficacy of Phenoxyethanol

Pseudomonas aeruginosa



	0.1 % Ethylhexylglycerin
	0.9 % Phenoxyethanol
	0.1 % Ethylhexylglycerin / 0.9 % Phenoxyethanol

Preservative Potentiators

Examples to be discussed:

- **EDTA**
- **Butylene Glycol**
- **1,3 Propanediol (Zemea)**

EDTA

(Ethylene-diamine-tetra-acetic acid)

- Is a chelator which works by binding trace metals which is needed for the survival of the organism
 - Has antimicrobial activity against gram negative bacteria
 - Also reported activity against fungus
 - Helps to prevent against antimicrobial resistance
- Helps in preventing discoloration, fragrance oxidation, cloudiness from metal ion impurities and product rancidity
 - Works well in an acid pH range
 - $\text{Na}^2\text{EDTA} > \text{Na}^3 > \text{Na}^4$

Butylene Glycol

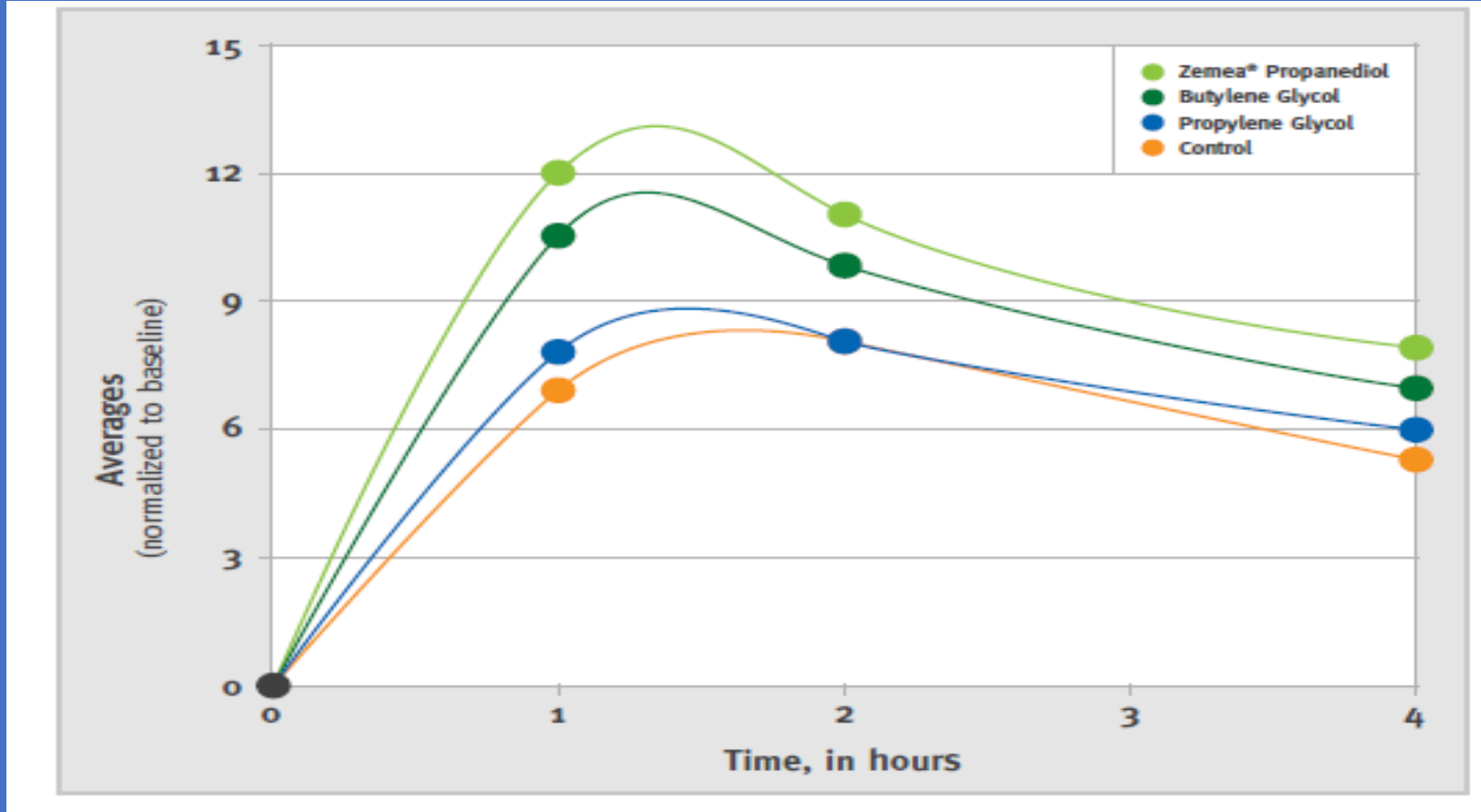
- Used to help stabilize emulsions
- Potentiates the activity of Parabens and Phenoxeyethanol
 - Helps solubilize and maintain preservatives in the water phase of an emulsion
 - Has bacteriostatic activity versus bactericidal activity
- Retards the loss of fragrances

Zemea Propanediol

- Zemea® Propanediol is a skin-friendly, corn derived natural glycol with enhanced performance benefits. Has humectant, solvent, emulsifier, and preservative booster, **due its anti-fungal / anti-microbial testing**
- CTFA Challenge Test data showed that Zemea® Propanediol has antimicrobial properties that prohibit contamination during shipping and handling.
- In the CTFA Challenge Test, Zemea® had similar performance to PG and BG in reduction of bacteria, yeast and mold.

Skin Hydration Study

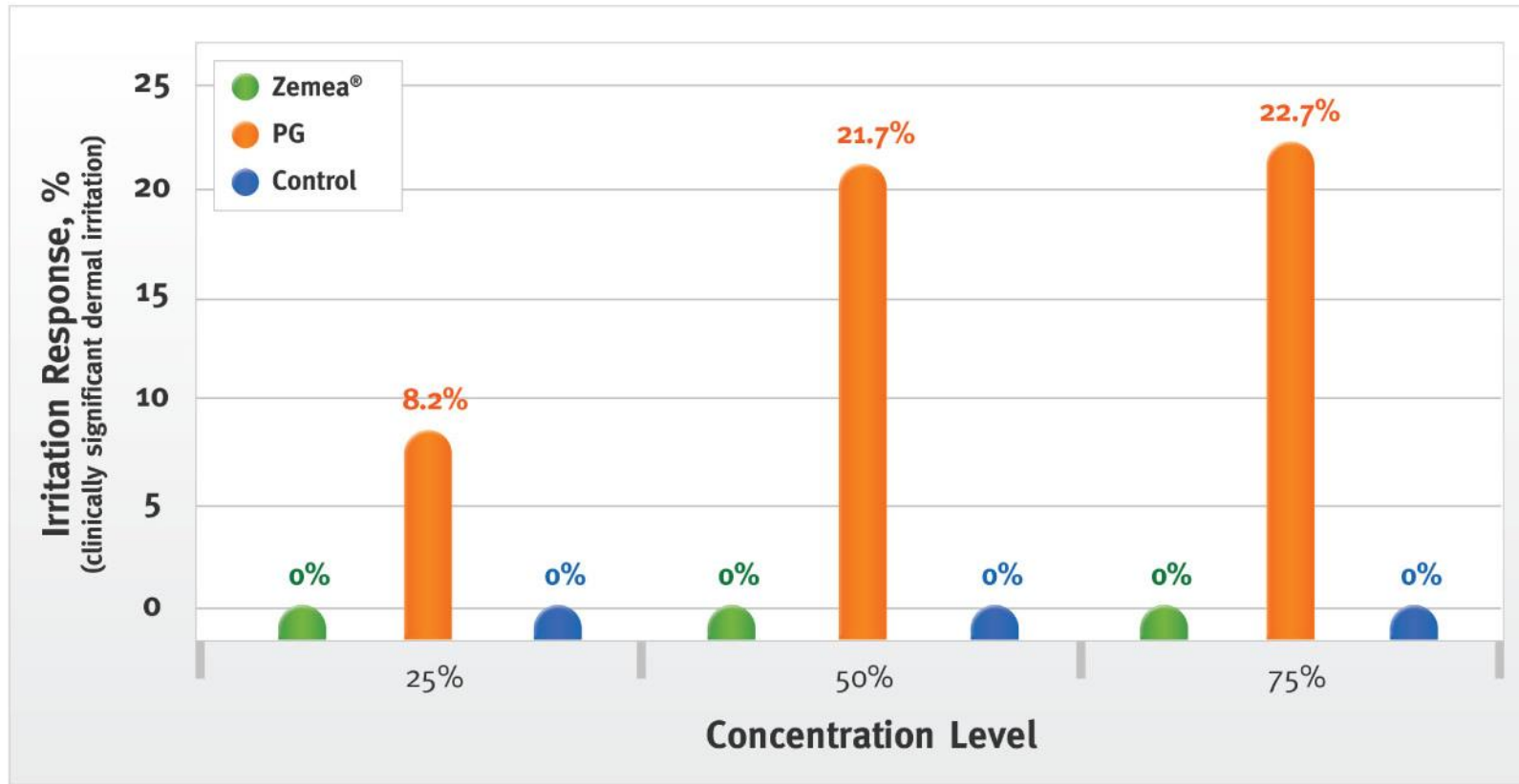
A skin hydration test was conducted on 10 female volunteers aged from 46 to 65. The 5 test creams were applied on the forearms of the volunteers who had dry skin on that area. The control cream replaced the glycol with water to evaluate the relative hydration properties of the other ingredients. A Corneometer 825 PC® (Courage & Khazaka) was used to measure skin hydration immediately after each application during the test.



Human Patch Studies

Human Skin Patch Test Results

(207 individuals exposed to Zemea® or Propylene Glycol or Control at 7pH)



At concentrations as high as 75%, **Zemea®** has not produced skin irritation or sensitization reactions.

Packaging and Risk Assessment

Microbiological Risk Assessment and Product Packaging

- In ISO 11930 – “**Evaluation of the Antimicrobial Protection of a Cosmetic Product**”, the guidelines uses Risk Assessment as part of the decision tree to ensure that if a product is safe even if it does not comply with the challenge test criteria. In this case protective packaging is used to ensure safety.

Atypical Products

- Formulation may not support microbial growth but the packaging system may be the vector or source of contamination.
- Clinical study or In-use study is the only way to measure potential risk and efficacy

Highest Risk *Potential*

Mascara Products

- Aqueous based
- Eye area product
- Multiple applications per day
- Standard Protocol
- Clinical Testing Required



Lowest Risk - Potential Lipsticks

- Anhydrous Hot Pour
- Applied on the lips
- No Potential for Microbial Growth
- No Testing Required



Highest Risk -Potential

- Atypical Product
- Anhydrous product
- Sponge tip applicator where risk resides
- Clinical Testing Required to test product – component interaction



Flow Through Pens

Low Risk Potential Powder Products

- Anhydrous product
- Brush application
- Product preserved
- Pass Challenge test at all phases of development -
Lower inoculum
- Clinical Use Testing and Micro Evaluation



High Risk - Potential

Wet / Dry Application

- Atypical Product
 - Anhydrous product being applied with a sponge tip applicator with water
 - Proper Preservation of all formulations
 - Safety-in-Use Testing and micro evaluation
 - Clinical-in-use testing of all applicators



Packaging;

A Major Role in Product Protection

- Prevent entry of bacteria, moisture, air, and product buildup.
Minimize consumer contact
- Applies to both storage of mass and finished product delivery
- Incorporation of sanitary or sterile filling procedures significantly reduces risk
- Can be incorporated with antimicrobial agent for added benefit

Dispensing Product: Airless Systems

- When filled in clean room, a sterile airless package needs minimal formula preservation.
- One-way valve insures product is dispensed without air return.
- More expensive package option.



Safety Considerations

- Superior protection from manufacture to shelf and continues to be safe in use.
- Contact points with skin may create risk.



Product Application: Brushes & Applicators

- “2nd Moment of Truth.”
- Application introduces bacteria to open/pour products.
- Most makeup brushes are made of goat or pony hair.
- New synthetics offer performance improvements.
 - Antimicrobial fiber.



Safety Considerations

- Natural hair promotes bacteria growth. Water-base formulas accelerate risk.
- Consumer don't wash as often as they think.
- Applicator contamination can be returned to the product. Brushes and applicators can be antimicrobial-treated.



Untreated



Treated, 100x wash

Product Application: Sponges & Puffs

- Mostly used for water-based formulas, or consumer adds water.
- Even when used with powders there can be enough water to form bacteria.
- Frequent and long duration product contact.

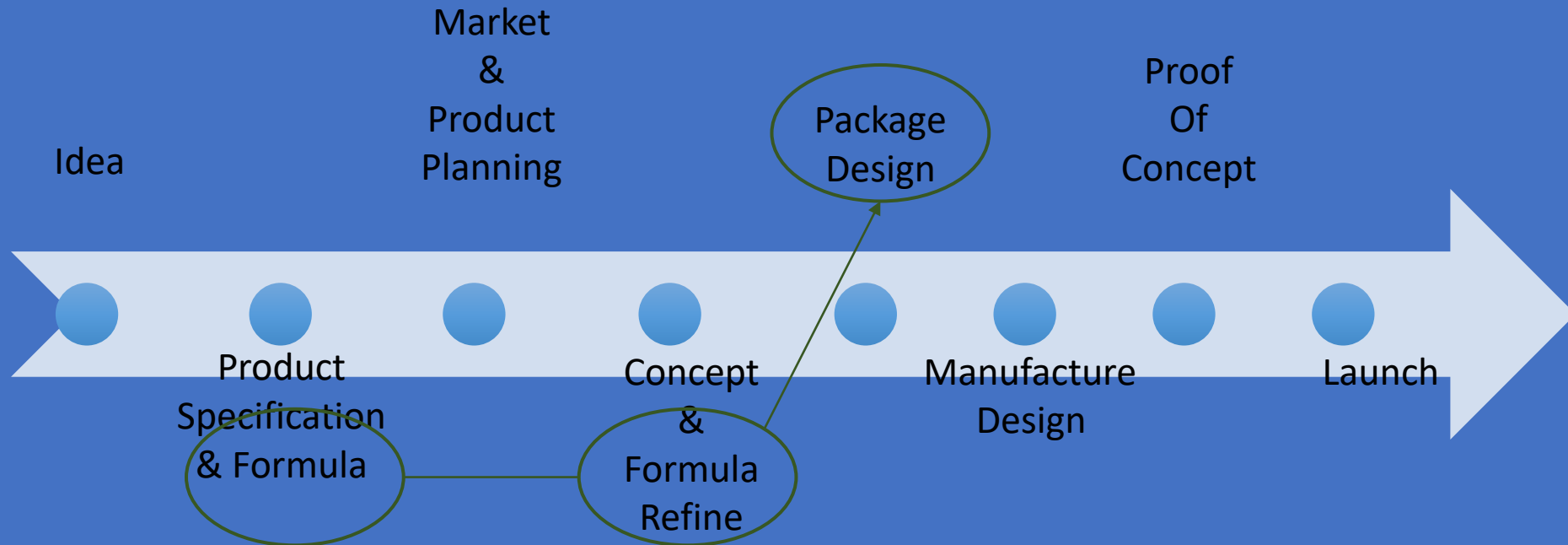
Safety Considerations

- Can be excellent host media for bacterial/mold/fungus growth.
- All sponges and puffs can be antimicrobial-treated.



Conclusion

Typical Product Development Process



Conclusion

- A Holistic approach towards product protection should be developed when creating new formulations
- The use of multi-functional ingredients can help in reducing the amount of a conventional preservatives to guarantee efficacy and safety.
- Be careful on making the preservative free claim
- Packaging can play a role in reducing potential risk but can also play a role in increasing risk in a certain product types
- Continued education in microbiology, preservation and formulation sciences should be pursued with those scientist entering into the marketplace