TECHNICAL BULLETIN

Zemea® Propanediol: An Effective Addition to Alcohol-based Hand Sanitizer Formulations

Introduction

The objective of this Technical Bulletin is to discuss the value-added benefits of using Zemea® Propanediol (1,3-Propanediol) as a multifunctional ingredient in alcohol-based hand sanitizer formulations versus glycerin and propylene glycol (PG).

Background

Hand sanitizer, also referred to as hand antiseptic or hand rub, is applied to the hands for the purpose of inactivating microorganisms and viruses. Inactivation of pathogenic microorganisms and viruses can have a beneficial impact on the prevention of disease. Hand sanitizers typically come in foam, gel, or liquid form. Their use is recommended when soap and water are not available for hand washing or when repeated hand washing compromises the natural skin barrier. Although the effectiveness of hand sanitizer is variable, it is employed as a simple means of infection control in a wide variety of settings, including day-care centers, schools, hospitals, health care clinics and from supermarkets to cruise ships.

Depending on the active ingredient used, hand sanitizers can be classified as one of two types: alcohol-based or alcohol-free. In fact, alcohol has been used as an antiseptic at least as early as 1363 with evidence to support its use becoming available in the late 1800s. Alcohol-based hand sanitizers has been commonly used in Europe since at least the1980s. For the purpose of this technical bulletin, we will focus our efforts solely on alcohol-based hand sanitizers

Alcohol-based products typically contain between 60 and 95 percent alcohol (v/v), usually in the form of ethanol, isopropanol, or *n*-propanol. At these concentrations, alcohol immediately denatures proteins, effectively neutralizing certain types of microorganisms. Additionally, many hand sanitizers also contain emollients (e.g. glycerin or 1,3-propanediol) that soothe the skin, thickening agents, and fragrance to mask the alcohol smell.

The effectiveness of hand sanitizer depends on multiple factors, including the way the product is applied (e.g., quantity used, duration of exposure, frequency of use) and whether the specific infectious agents present on a person's hands are susceptible to the active ingredient in the product. In general, alcohol-based hand sanitizers, if rubbed thoroughly over finger and hand surfaces for a period of 30 seconds, followed by complete air-drying, can effectively reduce populations of bacteria, fungi, and viruses (e.g., seasonal influenza and more recently COVID-19). Hand sanitizers can help control the transmission of infectious diseases, especially in settings where compliance with hand washing is poor. Likewise, in the workplace, the use of alcohol-based hand sanitizer has been associated with reductions in illness episodes and sick days. In hospitals and health care clinics, increased access to alcohol-based hand sanitizer has been linked to overall improvements in hand hygiene. Alcohol-based versions of hand sanitizers are on the World Health Organization's List of Essential Medicines, the safest and most effective medicines needed in a health system.

Safety

Agencies such as the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC) promote the use of alcohol-based hand sanitizers over alcohol-free products. Concerns over the use of alcohol-based hand sanitizer have centered primarily on product flammability and ingestion, both unintentional and intentional. With proper storage and strategies that limit access to alcohol-containing sanitizer (e.g., issuing hand sanitizer to individuals), the risk of fire or poisoning from accidental or intentional ingestion of alcohol-based hand sanitizers is considered to be low.

Research has shown that alcohol-based hand sanitizers do not pose any risk by eliminating beneficial microorganisms that are naturally present on the skin. The body and environment quickly replenish the beneficial microbes on the hands, often moving them in from just up the arms where there are fewer harmful microorganisms. However, alcohol may strip the skin of its outer, essential lipophilic components, which may have negative effects on barrier function of the skin such as invasion through the compromised skin by a multitude of nefarious microbes. A study also shows that disinfecting hands with an antimicrobial detergent result in a greater barrier disruption of skin compared to alcohol solutions, suggesting an increased loss of skin lipids.

Zemea® Propanediol

Zemea ® Propanediol is a natural, bio-based derived alternative to petroleum-based glycols for formulators who desire a multifunctional and innovative ingredient (**Figure 1**) that delivers high performance in a variety of consumer applications including cosmetics and personal care, food and flavors, pharmaceuticals, and laundry and household cleaners. It answers consumer demand for safe, pure, skin-friendly products. Zemea® propanediol functions well as an emollient, a humectant, an effective carrier of active ingredients, a preservative booster, a solubilizer, or a sensorial enhancer. Additionally, Zemea® propanediol is sustainably sourced and generates up to 40% less greenhouse gas emissions over its life, helping companies fulfill their sustainability goals without compromising on product quality.

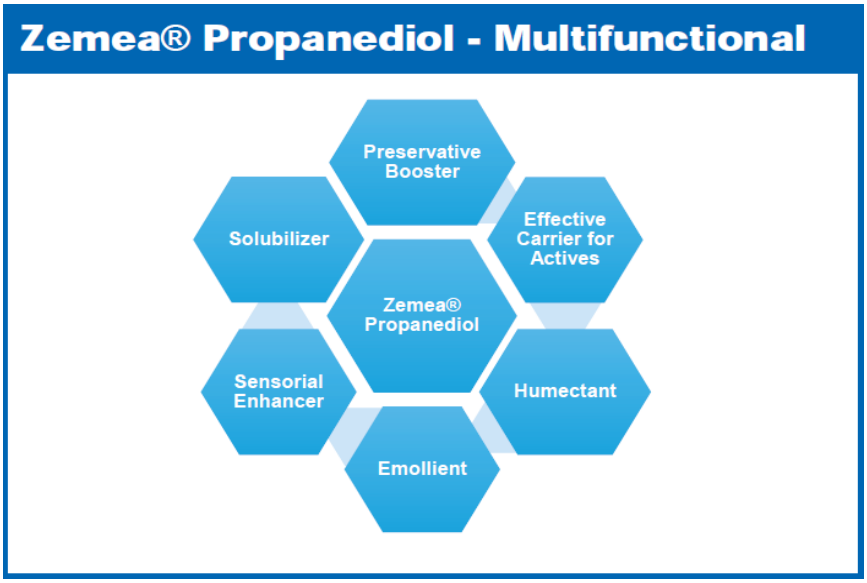

Figure 1: Zemea® Propanediol: A multifunctional ingredient making formulating easier.

Benefits of Zemea® Propanediol

- Improves humectancy.
- High purity, 99.9% propanediol, petroleum-free derived diol.
- Self-sterilizing, resistant to biological contamination, and does not support biological growth above concentrations of 20%.
- Excellent sensory characteristics
- 100% sustainably and renewably sourced
- More efficient than propylene glycol in moisturizing the skin (short term).
- Produces no clinically significant dermal irritation or sensitization (up to 75%) versus Propylene Glycol.
- Combined with glycerin (1:1 up to 1:4), reduces tackiness and viscosity of finished product.
- Combined with glycerin contributes to both short-term and longer-term skin moisturization and skin hydration.
- Higher boiling point (214ºC vs 188ºC) and lower vapor pressure (0.0119 mmHg vs 0.08 mmHg) than propylene glycol (PG), respectively leading to increased skin contact and effective work of the hand sanitizer.

Alcohol-based Hand Sanitizers

WHO Recommended Alcohol-based Hand Sanitizer formulations

To help countries and health-care facilities to achieve system change and adopt alcohol-based hand sanitizer as the gold standard for hand hygiene in health care, WHO has identified formulations for local preparation. Logistic, economic, safety, cultural and religious factors have all been carefully considered by the WHO before recommending such formulations for use worldwide. Ingredient considerations were made concerning cost constraints and microbicidal activity for the WHO-recommended hand sanitizer formulations. The following two formulations are recommended for local production with a maximum of 50 liters per lot to ensure safety in production and storage.

Formulation 1			**Formulation 2**		
Ethanol 80% *v/v*, Glycerol 1.45% *v/v*, Hydrogen Peroxide (H_2O_2) 0.125% *v/v*.			Isopropyl alcohol 75% *v/v*, glycerol 1.45% *v/v*, hydrogen peroxide 0.125% *v/v*:		
Ingredients	**Volume, mL**	**Vol %**	**Ingredients**	**Volume, mL**	**Vol %**
Ethanol, 96% v/v	**833.3**	**83.33**	**Isopropyl Alcohol, 99.8% v/v**	**751.5**	**75.15**
Hydrogen Peroxide, 3%	**41.7**	**4.17**	**Hydrogen Peroxide, 3%**	**41.7**	**4.17**
Glycerol, 98%	**14.5**	**1.45**	**Glycerol, 98%**	**14.5**	**1.45**
Distilled Water	**110.5**	**11.05**	**Distilled Water**	**192.3**	**19.23**
Total	**1000.0**	**100.00**	**Total**	**1000.0**	**100.00**

Table 1. WHO recommended Alcohol-based Hand Sanitizer formulations.

Notes:

1. Glycerol: used as humectant, but other emollients may be used for skin care, if they are cheap, widely available, miscible in water and alcohol, and do not contribute toxicity or promote allergic reactions.
2. Hydrogen peroxide: used to inactivate contaminating bacterial spores in the solution and is not an active substance for hand antisepsis.
3. Any further additive to both formulations should be clearly labelled and be non-toxic in case of accidental ingestion.
4. A colorant may be added to allow differentiation from other fluids, but should not add to toxicity, promote allergy, or interfere with antimicrobial properties. The addition of perfumes or dyes is not recommended due to risk of allergic reactions.
5. https://www.who.int/gpsc/information_centre/handrub-formulations/en/
6. **For US producers** are still subject to FDA over-the-counter (OTC) monographs for hand sanitizers for use in reducing microorganisms or viruses on the skin that potentially can cause disease or decreasing microorganisms or viruses on the skin. See "Safety and Effectiveness of Consumer Antiseptic Rubs; Topical Antimicrobial Drug Products for Over-the-Counter Human Use," Final Rule, 84 FR 14847 (April 12, 2019); "Safety and Effectiveness of Health Care Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use Final Rule," 82 FR 60474 (December 20, 2017); "Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products," Proposed Rule, 59 FR 31402 (June 17, 1994) (1994 TFM). https://www.fda.gov/media/136118/download.
    - Glycerol (glycerin) United States Pharmacopeia (USP) or Food Chemical Codex (also known as "food grade")

Zemea® Propanediol is widely used in cosmetic and personal care applications, including hand sanitizers, for improved humectancy, product stability, hydration, and skin texture. **Figure 1** illustrates testing conducted by Ellead Skin and BIO Research on 20 subjects measuring the loss of moisture using an Epsilon BioX for simple solutions applied to forearm containing Zemea® (10 wt.%), Zemea® (5 wt.%)/Glycerin (5 wt.%) BDO (10 wt%), and DPG (10 wt.%). The results compared treated skin areas for which the blend of glycerol (glycerin) and Zemea® Propanediol preformed the best in terms of skin moisturization. To take advantage of the benefits of Zemea® Propanediol and to capitalize on the synergistic effect characteristics experienced when blending Zemea® Propanediol with glycerol (glycerin) in terms of skin feel and moisturization, hand sanitizer formulations are presented (**Table 2 and Table 3**) as blends of glycerol and Zemea® Propanediol (1,3-propanediol) where the addition of Zemea® Propanediol is an emollient used in skin care, is widely available, is miscible in water and alcohol and does not contribute toxicity or allergens to the core formulation (see Notes 1-5 above).

Furthermore, Zemea® Propanediol is used interchangeably with in cosmetic and personal care products to provide benefits related to this class of 3-carbon polyol compounds (glycerin, propylene glycol, and 1,3-propanediol). We are compliant with the FDA Guidance (Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Immediately in Effect Guidance for Industry, https://www.fda.gov/media/136118/download) with respect to improving the smell or taste of the hand sanitizer formulation that includes Zemea® Propanediol. Zemea® USP-FCC Propanediol is included on the U.S. FDA GRAS inventory (GRN 000302, https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=GRASNotices&id=302). Additionally, glycerol and 1,3-propanediol are similar in chemical properties including organoleptic properties (Glycerol, https://pubchem.ncbi.nlm.nih.gov/compound/753 and Propanediol, https://pubchem.ncbi.nlm.nih.gov/compound/10442), chemical structure and functionality.

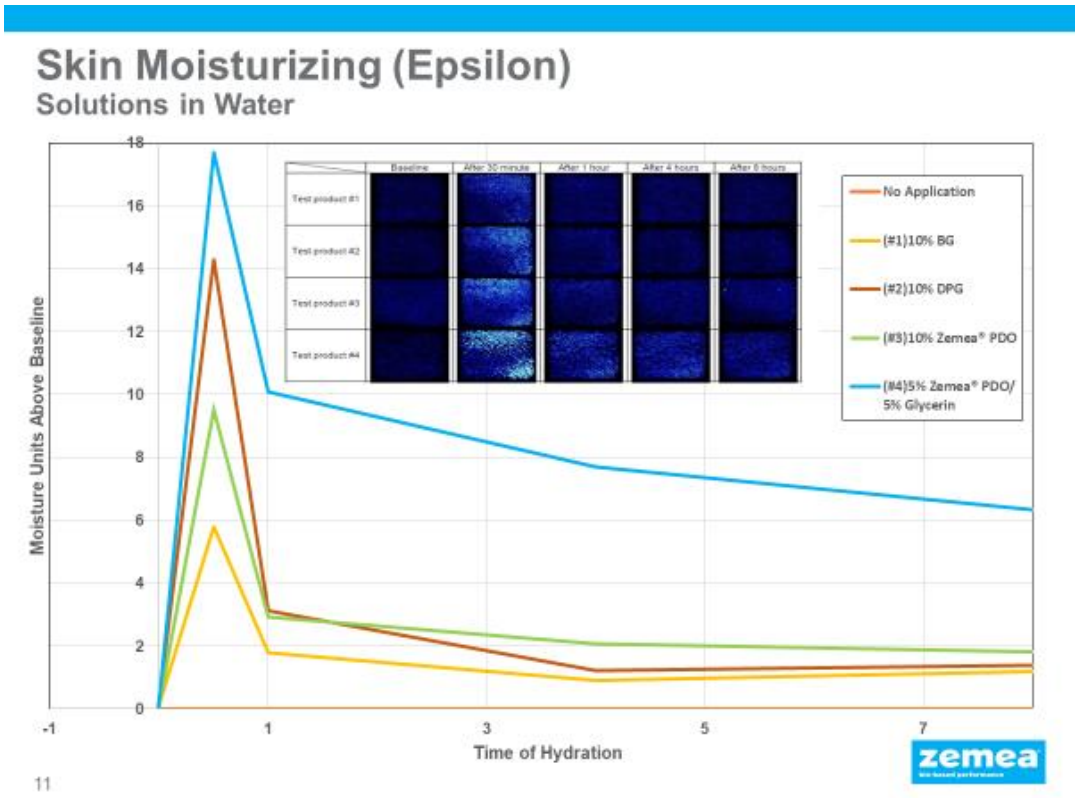

Figure 1. Skin Moisturizing Performance: Moisture above baseline versus Time of Hydration.

Hand Sanitizer Formulations including Zemea® Propanediol

Formulation 3			**Formulation 4**		
Ethanol 80% *v/v*, Glycerol 1.45% *v/v*, Zemea® PDO 2.50 v/v, Hydrogen Peroxide (H_2O_2) 0.125% *v/v*.			Ethanol 80% *v/v*, glycerol 1.45% *v/v*, Zemea® PDO 5.00 v/v, Hydrogen peroxide 0.125% *v/v*:		
Ingredients	**Volume, mL**	**Vol %**	**Ingredients**	**Volume, mL**	**Vol %**
Ethanol, 96% v/v	**833.3**	**83.33**	**Ethanol, 96% v/v**	**833.3**	**83.33**
Hydrogen Peroxide, 3%	**41.7**	**4.17**	**Hydrogen Peroxide, 3%**	**41.7**	**4.17**
Glycerol, 98%*	**14.5**	**1.45**	**Glycerol, 98%***	**14.5**	**1.45**
Zemea® PDO, 99.8%*	**25.0**	**2.50**	**Zemea® PDO, 99.8%***	**50.0**	**5.00**
Distilled Water	**85.5**	**8.55**	**Distilled Water**	**60.5**	**6.05**
Total	**1000.0**	**100.00**	**Total**	**1000.0**	**100.00**

Table 2. Ethanol-based Hand Sanitizer formulations including Zemea® Propanediol

***** US Producers refer to FDA Guidance **(**https://www.fda.gov/media/136118/download) and use UPS or FCC grades for glycerol and propanediol.

Formulation 5			Formulation 6		
IPA 75% *v/v*, Glycerol 1.45% *v/v*, Zemea® PDO 2.50 v/v, Hydrogen Peroxide (H_2O_2) 0.125% *v/v*.			IPA 75% *v/v*, Glycerol 1.45% *v/v*, Zemea® PDO 5.00 v/v, Hydrogen peroxide 0.125% *v/v*:		
Ingredients	**Volume, mL**	**Vol %**	**Ingredients**	**Volume, mL**	**Vol %**
IPA, 99.8% v/v	**751.5**	**75.15**	**IPA, 99.8% v/v**	**751.5**	**75.15**
Hydrogen Peroxide, 3%	**41.7**	**4.17**	**Hydrogen Peroxide, 3%**	**41.7**	**4.17**
Glycerol, 98%*	**14.5**	**1.45**	**Glycerol, 98%***	**14.5**	**1.45**
Zemea® PDO, 99.8%*	**25.0**	**2.50**	**Zemea® PDO, 99.8%***	**50.0**	**5.00**
Distilled Water	**167.3**	**16.73**	**Distilled Water**	**142.3**	**14.23**
Total	**1000.0**	**100.00**	**Total**	**1000.0**	**100.00**

Table 3. Isopropanol-based Hand sanitizer formulations including Zemea® Propanediol.

* US Producers refer to FDA Guidance (https://www.fda.gov/media/136118/download) and use UPS or FCC grades for glycerol and propanediol

Conclusions:

- Zemea® propanediol is a high performing, multifunctional, natural ingredient suited for hand sanitizer applications.
- Zemea® propanediol can provide good skin feel with reduced tackiness, improved humectancy for short-term and long-term skin moisturization and hydration benefits when blending with glycerol (glycerin).
- Zemea® propanediol is a material that is characterized as self-sterilizing and resistant to biological contamination, thus making it ideal for hand sanitizer applications.

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