COVID-19: HAND SANITISER INGREDIENTS

Author: Dr Micah DJ Peters **Date:** March 30 2020

Question: What is the best available evidence regarding the necessary active ingredients of hand sanitiser in the context of COVID-19?

***ALERT* Evidence regarding COVID-19 is continually evolving. This Evidence Brief will be updated regularly to reflect new emerging evidence but may not always include the very latest evidence in real-time.**

Key messages:

- To be effective and recommended for use hand sanitiser, hand rub should contain either ethanol 80% v/v (pharmacopoeial grade or food standard grade) OR isopropyl alcohol 75% v/v (pharmacopoeial grade) in an aqueous solution.
- Other preparations are not recommended as effective hand rubs.
- Washing hands with soap is the most effective way to practice good hand hygiene during the COVID-19 pandemic and may be supplemented by the use of recommended hand sanitisers.
- Products such as 'Safe T Guard' should not be recommended substitutes for hand rubs that contain the above proportions of ethanol or isopropyl alcohol.

Summary

Hand sanitisers may come in the form of a hand rub or hand wash. A hand rub is usually formulated as an alcohol-based gel or solution that is intended to be used on hands without the use of water in a hand rubbing procedure. A hand wash is a detergent-based formulation intended to be used with water in a hand washing procedure.

Background

COVID-19 pandemic

COVID-19 (from 'severe acute respiratory syndrome coronavirus 2' (or 'SARS-CoV-2') is a newly discovered (novel) corona virus first identified in Wuhan, Hubei province, China in 2019 as the cause of a cluster of pneumonia cases.[1] Coronaviruses are similar to a number of human and animal pathogens including some of those which cause the common cold as well as more serious illnesses including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Since discovery, COVID-19 has spread to many countries and was declared a pandemic on January 30, 2020.[2]

Summary of Evidence

Recommended hand sanitiser preparations

The World Health Organization (WHO) has identified formulations for the local preparation of alcohol-based hand rub formulations and notes that at present, alcohol-based hand rubs are the only known means for rapidly and effectively inactivating a wide array of potentially harmful microorganisms on hands.3 The following two formulations are recommended by the WHO for local production with a maximum of 50 litres per lot to ensure safety in production and storage:

1. **Formulation 1:** To produce final concentrations of ethanol 80% *v/v,* glycerol 1.45% *v/v,* hydrogen peroxide (H2O2) 0.125% *v/v.*
2. **Formulation 2:** To produce final concentrations of isopropyl alcohol 75% *v/v,* glycerol 1.45% *v/v,* hydrogen peroxide 0.125% *v/v.*

The Australian Government Department of Health's Therapeutic Goods Administration (TGA) outlines the requirements for Australian market authorisation of hand sanitisers (hand rubs or hand washes) when applied for as an over-the-counter (OTC) New Medicine N2 application.[4] Proposed medicines must comply with all aspects of the TGA's monograph relevant to their strength and dosage form to qualify for evaluation as an N2 application. The TGA's monograph also only applies to medicines containing ethanol, isopropyl alcohol, chlorhexidine gluconate, and triclosan either alone or in combination with one another as active ingredients. The TGA accepts the following dosage forms and strengths for hand rub and wash:[4]

Active substance	Dosage forms	Dosage strengths
Ethanol	Lotion, gel or solution formulated as a hand rub	60-95% v/v absolute ethanol
Isopropyl alcohol	Lotion, gel or solution formulated as a hand rub	60-95% v/v
A combination of ethanol and isopropyl alcohol	Lotion, gel or solution formulated as a hand rub	Total alcohol content of 60-95% v/v
Chlorhexidine gluconate	Solution when formulated as a hand wash	1-2% w/v
Combination of ethanol and chlorhexidine gluconate	Lotion, gel or solution formulated as a hand rub	60-95% v/v absolute ethanol with 0.5-2% w/v chlorhexidine gluconate
Combination of isopropyl alcohol and chlorhexidine gluconate	Lotion, gel or solution formulated as a hand rub	60-95% v/v isopropyl alcohol with 0.5-2% w/v chlorhexidine gluconate
Triclosan	Solution when formulated as a hand wash	1% w/v

Based on laboratory evidence, the United States Centers for Disease Control and Prevention (CDC) recommended that 60% ethanol and 70% isopropanol, the active ingredients in CDC-recommended alcohol-based hand sanitisers, inactivates viruses that are genetically related to, and with similar physical properties as, the 2019-nCoV.[5]

In Australia on 28 March 2020, specified hand sanitiser formulations were excluded from TGA regulation as long as they only contain particular ingredients in particular quantities in the final formulation, and comply with certain manufacturing practices, and advertisement and labelling conditions.[6] Provided that the exact formulation and other requirements are followed, this formulation is permitted for use in both healthcare facilities and consumer use. The formulations are based on advice by the World Health Organization and similar decisions by the US Food and Drug Administration. The final formulation of the hand sanitiser must contain only the following ingredients:

- EITHER ethanol 80% v/v (pharmacopoeial grade or food standard grade) OR isopropyl alcohol 75% v/v (pharmacopoeial grade) in an aqueous solution;
- sterile distilled water or boiled cold water;
- glycerol 1.45% v/v (pharmacopoeial grade);
- hydrogen peroxide 0.125% v/v (pharmacopoeial grade); and
- does not contain any other active or inactive ingredients, including colours, fragrances or emollients.

Not recommended preparations

Other preparations exist that are marketed as 'hand sanitisers' that do not contain the above ingredients in the recommended proportions. Such products may be considered 'cosmetics'.[6] One such product produced by Jasol named 'Safe T Guard' contains the following ingredients and proportions:[7]

Name	**Proportion**
Aqua	95- 99 %
COCAMIDOPROPYL PG- DIMONIUM CHLORIDE PHOSPHATE	0. 1- 1 %
Benzalkonium chloride	0. 1- 1 %
Chlorhexidine digluconate	<0. 2 %
Glycerin	<0. 1 %
Triethylene glycol	<0. 1 %

Safe T Guard is marketed for use as an alcohol free foaming hand sanitiser for use in food processing areas and healthcare and is designed to be used after washing hands to kill pathogenic and food spoilage bacteria and other organisms.[8] While Safe T Guard contains ingredients that have some antimicrobial properties, these are not in sufficient proportions to be effective as a virucidal or bactericidal preparation in the context of COVID-19.

Benzalkonium chloride is a biocidal agent that is used for surface disinfection. A recent study however stated that at concentrations between 0.05-0.2% benzalkonium chloride is unlikely to be effective. Data obtained with benzalkonium chloride at reasonable contact times have been conflicting. Within ten minutes, a concentration of 0.2% revealed no efficacy against coronaviruses whereas a concentration of 0.05% was quite effective.[9] This perspective is supported by the United States Centers of Disease Control (CDC) which does not have a recommended alternative to hand rub products with greater than 60% ethanol or 70% isopropanol as active ingredients. The CDC highlights that available evidence indicates benzalkonium chloride has less reliable activity against coronavirus than either of the alcohols.[10]

Safe T Guard contains chlorhexidine digluconate which is the salt form of chlorhexidine. This chemical is a bisbiguanide antiseptic and disinfectant, which is bactericidal or bacteriostatic against a wide range of gram negative and gram-positive vegetative bacteria, yeasts, dermatophyte fungi and lipophilic viruses. It is important to note that the proportion of chlorhexidine digluconate in Safe T Guard is considerably less than that which is recommended by the TGA and is therefore unlikely to provide adequate virucidal or bactericidal activity as a hand rub.

Triethylene glycol is another ingredient with antimicrobial properties that is used as bacteriostat (against odour-causing bacteria) for air sanitisation and deodorisation, disinfection of hard, non-porous surfaces in combination with other ingredients, and as an insecticide (against lice).[11] It is also used in cosmetic formulations, with a maximum concentration of use of 0.08% in skin-cleansing products.[12] Early studies into triethylene glycol noted that bactericidal activity does not become apparent until concentrations of over 20% are reached.[13]

References

1. World Health Organization. Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 (accessed Mar 25 2020).
2. World Health Organization. Rolling updates on coronavirus disease (COVID-19). 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen (accessed Mar 25 2020).
3. World Health Organization. WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care Is Safer Care. 2009. https://www.ncbi.nlm.nih.gov/books/NBK144054/ (accessed 30 Mar 2020).
4. Australian Government Department of Health Therapuetic Goods Administration. OTC Medicine Monograph: Hand Sanitisers. 15 Sept 20215 2020. https://www.tga.gov.au/otc-medicine-monograph-hand-sanitisers (accessed 30 Mar 2020 2020).
5. Centers for Disease Control and Prevention. CDC Statement for Healthcare Personnel on Hand Hygiene during the Response to the International Emergence of COVID-19. 2020. https://www.cdc.gov/coronavirus/2019-ncov/infection-control/hcp-hand-sanitizer.html (accessed 30 Mar 2020).
6. Australian Government Department of Health Therapuetic Goods Administration. Hand sanitisers and COVID-19. 2020. https://www.tga.gov.au/hand-sanitisers-and-covid-19 (accessed 30 Mar 2020).
7. Jasol. Safety Data Sheet: Safe T Guard. 16 May 20218 2016. http://www.csinfosafe.com/CSIAU/SDSIndex.aspx?flag=init (accessed 30 Mar 2020).
8. Washroom Accessories. Jasol Safe T Guard 2073750 Foaming hand sanitiser, alcohol free. 2007. https://www.washroomaccessories.com.au/jasol/7059-2073750-alcohol-free-foaming-hand-sanitiser-.html (accessed 30 mar 2020).
9. Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *Journal of Hospital Infection* 2020; 104(3): 246-51.
10. Centers for Disease Control and Prevention. Frequently Asked Questions about Hand Hygiene for Healthcare Personnel Responding to COVID-2019. 2020. https://www.cdc.gov/coronavirus/2019-ncov/infection-control/hcp-hand-hygiene-faq.html (accessed 30 Mar 2020).
11. United States Environmental Protection Agency. Reregistration Eligibility Decision (RED) for Triethylene Glycol. Washington D.C.: United States Environmental Protection Agency 2003.
12. No Authors Listed. Final report on the safety assessment of Triethylene Glycol and PEG-4. *International journal of toxicology* 2006; 25 Suppl 2: 121-38.
13. Lester W, Jr., Kaye S, Robertson OH, Dunklin EW. Factors of importance in the use of triethylene glycol vapor for aerial disinfection. *Am J Public Health Nations Health* 1950; 40(7): 813-20.