THE FIRST GLOBAL PATIENT SAFETY CHALLENGE
Clean Care is Safer Care

A WHO Alcohol-based Handrub Formulation

According to the available evidence on efficacy, tolerability and cost-effectiveness, WHO recommends using an alcohol-based handrub for routine hand antisepsis in most clinical situations. Health care settings currently using commercially-available handrubs, liquid soaps and skin care products sold in disposable containers should continue this practice, provided that the handrubs meet recognised standards for microbiological efficacy (ASTM or EN standards) and are well accepted by the health-care workers. In health care settings where these products are not available or too costly, production of the WHO handrub according to the formula and methodology suggested below is an alternative.

Suggested composition of alcohol-based formulations for in-house/local production

The choice of components for the WHO handrubs takes into account both cost constraints and microbiological efficacy. As just mentioned, the use of commercially-available products which meet recognized standards (ASTM or EN) and are well accepted by the health-care workers can be continued, even if their ingredients differ from that of the WHO formulations described below. The following two alcohol-based handrub formulations are recommended for preparation in-house or in a local production facility, up to a maximum of 50 litres:

Formulation I

To produce final concentrations of ethanol 80% v/v, glycerol 1.45% v/v, hydrogen peroxide 0.125% v/v.

Pour into a 1000 ml graduated flask:

a) ethanol 96% v/v 833.3 ml

b) hydrogen peroxide 3% 41.7 ml

c) glycerol 98% 14.5 ml

Top up the flask to 1000 ml with distilled or boiled and cooled water and shake the flask gently to mix the content.

Formulation II

To produce final concentrations of isopropyl alcohol 75% v/v, glycerol 1.45% v/v, hydrogen peroxide 0.125% v/v:

Pour into a 1000 ml graduated flask:

a) isopropyl alcohol (with a purity of 99.8%) 751.5 ml

b) hydrogen peroxide 3% 41.7 ml

c) glycerol 98% 14.5 ml

Top up the flask to 1000 ml with distilled or boiled and cooled water and shake the flask gently to mix the content.

Points to note:

Safety Standards

The recommended handrub formulations have been tested for efficacy according to international norms in WHO-designated independent laboratories. With regard to skin reactions, handrubbing with alcohol-based solutions is better tolerated than handwashing with soap and water. Any additive should be as non-toxic as possible in case of accidental or intentional ingestion.

- Distribution
  - Disposable bottles should preferably be used even though reusable sterilizable bottles may reduce production costs and waste management.
  - To prevent evaporation, containers should have a maximum capacity of 500 ml on wards and 1 litre in operating theatres, and ideally fit into a wall dispenser.
  - Leakage-free pocket bottles with a capacity of no more than 100 ml should also be available and distributed individually to health-care workers with emphasis that their use should be confined to health care only.
  - The production or re-filling units should follow norms on how to clean and disinfect the bottles (e.g. autoclaving, boiling, or chemical disinfection with chlorine). Autoclaving is considered the most suitable procedure. Reusable bottles should never be refilled until they have been completely emptied and then cleansed and disinfected.
- Cleansing and disinfection process for reusable handrub bottles:
  - I. bring empty bottles to a central point for reprocessing by standard operational protocols;
  - II. wash bottles thoroughly with detergent and tap water to eliminate any residual liquid;
  - III. if heat-resistant, thermally disinfect bottles by boiling in water. Whenever possible, thermal disinfection should be chosen in preference to chemical disinfection. The latter may increase costs and introduces an extra step to flush out the remains of the disinfectant. Chemical disinfection should include soaking the bottles in a solution containing 1000 ppm of chlorine for a minimum of 15 minutes and then rinsing with sterile/cooled boiled water;
  - IV. after thermal or chemical disinfection, leave bottles to dry completely upside-down in a bottle rack. Dry bottles should be closed with a lid and stored, protected from dust, until use.

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Guide to in-house manufacturing

10 litre preparations: glass or plastic bottles with screw-threaded stoppers can be used.

50 litre preparations: large plastic (preferably polypropylene, translucent enough to see the liquid level) or stainless steel tanks with a 80 to 100 litres capacity should be used to allow for mixing without overflowing.

The tanks should be calibrated for the ethanol/isopropyl alcohol volumes and for the final volumes of either 10 or 50 litres. It is best to mark

plastic tanks on the outside and stainless steel ones on the inside.

Mixing should be carried out using wooden, plastic or metallic paddles. Electric mixers should not be used unless "EX" protected because of

danger of explosion.

Preparation

1) The alcohol for the chosen formula is poured into the large bottle or tank up to the graduated mark.
2) Hydrogen peroxide is added using the measuring cylinder.
3) Glycerol is added using a measuring cylinder. As the glycerol is very viscous and sticks to the walls of the measuring cylinder, it can be rinsed with some of the water to be added and emptied into the tank.
4) The tank is then topped up to the corresponding mark of the volume to be prepared with the remainder of the distilled or cooled, boiled water.
5) The solution is mixed by gently shaking the recipient where appropriate (small quantities) or by using a paddle.
6) The lid or the screw cap is placed on the tank/bottle immediately after mixing to prevent evaporation.

For a more detailed production guideline for 10 and 50 litres of both formulations see the "Guide to in-house/local manufacturing" at www.who.int/patientsafety

After dividing the solution into smaller containers (e.g., 1000, 500 or 100 ml plastic bottles), the bottles should be put into quarantine for 72 hours.

This allows time for any spores present in the alcohol or the (re-used) bottles to be destroyed by the hydrogen peroxide.

Note: If concentrated alcohol is obtained from local production, verify the alcohol concentration and make the necessary adjustments in volume to obtain the final recommended concentration.

Labelling of the bottles should be in accordance with national guidelines, but should include the mention of:

- antiseptic handrub solution
- for external use only
- keep out of reach of children
- avoid contact with eyes
- use: apply about 2 ml to the palm of the hand and rub both hands and fingers, front and back until dry.
- formula contents:

  Formulation I

  Ethanol 80% (v/v), glycerol 1.45% and hydrogen peroxide 0.125%

  or

  Formulation II

  Isopropyl alcohol 75% (v/v), glycerol 1.45% and hydrogen peroxide 0.125%
- flammable liquid: keep away from heat and flames.

Special requirements are applicable for the production and storage of the formulations, as well as the storage of the primary products. The quantity of locally-produced WHO handrub should not exceed 50 litres, or possibly less if regulated by local and/or national guidelines and regulations.

Alcohol is the active component and some aspects concerning other components should be respected. All components should be free of spores [i.e. by treatment with hydrogen peroxide (H_2O_2) or, commercially, by filtering]. While the use of H_2O_2 autosterilizes the solution, i.e. of spores originating from components or reused bottles, and thereby adds an important safety aspect, the use of 3–6% of H_2O_2 for the production might be complicated by its corrosive nature and difficult procurement in some countries.

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While the chance of ingestion should be reduced, i.e. by a bad taste additive such as methylethylketone (1% in 96% ethanol), this would increase the toxicity of the product in cases of accidental ingestion, as well as adding costs and problems of availability. For this reason, no bad taste additive is included in the above formulations. Any further additive to both formulations should be clearly labelled and non-toxic in case of accidental ingestion. A colorant may be added to allow differentiation from other fluids, but should not add to toxicity, promote allergy, or interfere with antimicrobial properties. Formulations should be labelled adequately in accordance with national guidelines.

To further reduce the risk of ingestion and to promote use of the product in regions where even external alcohol use may be considered problematic because of cultural or religious reasons, the product name should avoid the term "alcohol" and should be referred to as a handrub with antimicrobial properties. Both recommended formulations should be produced in a liquid form. Addition of gelling agents may increase production costs and, in some cases, reduce antimicrobial efficacy.

While sterile distilled water is the preferable component for production of the formulations, cooled, boiled water may also be used.

Glycerol is added to the formulation as a humectant to increase the acceptability of the product. Other humectants or emollients may be used as long as they are non-toxic, cheap, widely available, do not cause allergies, and are miscible (mixable) in water and alcohol. Glycerol was chosen because of its historical safety record.

The WHO handrub formulations can be used for hygienic hand antisepsis and for surgical hand preparation. According to EN standards, the efficacy of the formulations is equivalent to the reference substance for hygienic hand antisepsis, whereas for surgical hand preparation, it is slightly lower. Further results according to both the EN and ASTM standards will be available in the near future. Substances such as chlorhexidine could be added to achieve a sustained effect, but this would complicate production and increase costs. For hygienic hand antisepsis, a sustained effect is not required.

Within the implementation strategy, the use of the WHO formulations at country level should undergo a pilot phase in a limited number of sites to evaluate feasibility and acceptability.

Production facilities and cost issues

Manufacture of the WHO handrub formulation should be possible in production units such as central pharmacies or dispensaries. According to local policies, governments should make every effort to encourage local production, support the quality assessment process and keep production costs as low as possible. Since undiluted ethanol is highly flammable and may ignite at temperatures as low as 10°C, production facilities should directly dilute it to the above-mentioned concentration. The flash points of ethanol 80% (v/v) and of isopropyl alcohol 75% (v/v) are 24°C and 18°C, respectively, and special attention should be given to proper storage in tropical climates. National safety guidelines and local legal requirements have to be considered in the storage of ingredients and the final product. The WHO handrub formulations should not be produced in quantities above 50 litres locally or in central pharmacies lacking specialised air conditioning and ventilation. There should be no smoking or naked flames in production and storage areas.

The costs of the WHO handrub formulation may vary according to country, resources and labour costs; studies to evaluate costs and resource use are necessary. As a comparison, examples of actual prices of commercially available alcohol-based handrubs in different countries are detailed within the Guidelines.

The WHO Information Sheet on the production of an antiseptic handrub describes a WHO recommendation for alcohol-based handrub formulations to facilitate local production.

This is Information sheet 5 in a series of 7 related to the Clean Care is Safer Care Challenge
The leaflets are based on the WHO Guidelines on Hand Hygiene in Health Care (Advanced Draft)
For further information about Clean Care is Safe Care, please contact the Secretariat of the World Alliance for Patient Safety,
e-mail: patientsafety@who.int or for a full list of tools visit: www.who.int/gpsc/en/index.html

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