World Health Organization

Patient Safety

A World Alliance for Safer Health Care

SAVE LIVES
Clean **Your** Hands

Guide to Local Production:
WHO-recommended Handrub Formulations

Introduction: This Guide to Local Production of WHO-recommended Handrub Formulations is separated into two discrete but interrelated sections:

Part A provides a practical guide for use at the pharmacy bench during the actual preparation of the formulation. Users may want to display the material on the wall of the production unit.

Part B summarizes some essential background technical information and is taken from WHO Guidelines on Hand Hygiene in Health Care (2009). Within Part B the user has access to important safety and cost information and supplementary material relating to dispensers and distribution.

Revised April 2010

PART A: GUIDE TO LOCAL PRODUCTION

Part A is intended to guide a local producer in the actual preparation of the formulation.

Materials required (small volume production)

REAGENTS FOR FORMULATION 1:	REAGENTS FOR FORMULATION 2:
• Ethanol 96%	• Isopropyl alcohol 99.8%
• Hydrogen peroxide 3%	• Hydrogen peroxide 3%
• Glycerol 98%	• Glycerol 98%
• Sterile distilled or boiled cold water	• Sterile distilled or boiled cold water

- 10-litre glass or plastic bottles with screw-threaded stoppers (1), or
- 50-litre plastic tanks (preferably in polypropylene or high density polyethylene, translucent so as to see the liquid level) (2), or
- Stainless steel tanks with a capacity of 80–100 litres (for mixing without overflowing) (3 , 4)
- Wooden, plastic or metal paddles for mixing (5)
- Measuring cylinders and measuring jugs (6 , 7)
- Plastic or metal funnel
- 100 ml plastic bottles with leak-proof tops (8)
- 500 ml glass or plastic bottles with screw tops (8)
- An alcoholometer: the temperature scale is at the bottom and the ethanol concentration (percentage v/v) at the top (9 , 10 , 11)

NOTE

- Glycerol: used as humectant, but other emollients may be used for skin care, provided that they are cheap, widely available and miscible in water and alcohol and do not add to toxicity, or promote allergy.
- Hydrogen peroxide: used to inactivate contaminating bacterial spores in the solution and is not an active substance for hand antisepsis.
- Any further additive to both formulations should be clearly labelled and be 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. The addition of perfumes or dyes is not recommended due to risk of allergic reactions.


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METHOD: 10-LITRE PREPARATIONS

These can be prepared in 10-litre glass or plastic bottles with screw-threaded stoppers.

Recommended amounts of products:

FORMULATION 1	FORMULATION 2
• Ethanol 96%: **8333 ml** • Hydrogen peroxide 3%: **417 ml** • Glycerol 98%: **145 ml**	• Isopropyl alcohol 99.8%: **7515 ml** • Hydrogen peroxide 3%: **417 ml** • Glycerol 98%: **145 ml**

Step by step preparation:

1. The alcohol for the formula to be used is poured into the large bottle or tank up to the graduated mark.

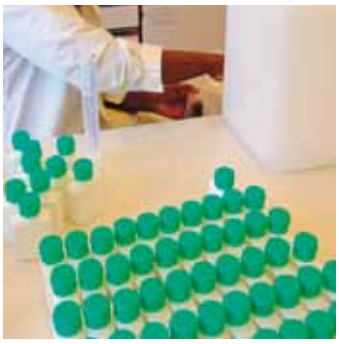
4. The bottle/tank is then topped up to the 10-litre mark with sterile distilled or cold boiled water.

5. The lid or the screw cap is placed on the tank/bottle as soon as possible after preparation, in order to prevent evaporation.

2. Hydrogen peroxide is added using the measuring cylinder.

6. The solution is mixed by shaking gently where appropriate or by using a paddle.

3. Glycerol is added using a measuring cylinder. As glycerol is very viscous and sticks to the wall of the measuring cylinder, it should be rinsed with some sterile distilled or cold boiled water and then emptied into the bottle/tank.



7. Immediately divide up the solution into its final containers (e.g. 500 or 100 ml plastic bottles), and place the bottles in quarantine for 72 hours before use. This allows time for any spores present in the alcohol or the new/re-used bottles to be destroyed.

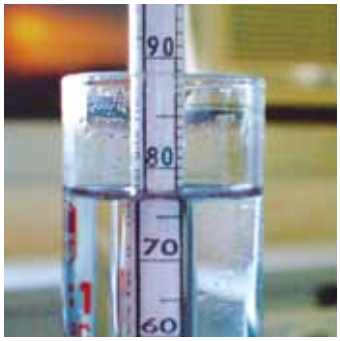
Final products

FORMULATION 1	FORMULATION 2
Final concentrations: • Ethanol 80% (v/v), • Glycerol 1.45% (v/v), • Hydrogen peroxide 0.125% (v/v)	**Final concentrations:** • Isopropyl alcohol 75% (v/v), • Glycerol 1.45% (v/v), • Hydrogen peroxide 0.125% (v/v)

Quality control

1. Pre-production analysis should be made every time an analysis certificate is not available to guarantee the titration of alcohol (i.e. local production). Verify the alcohol concentration with the alcoholmeter and make the necessary adjustments in volume in the preparation formulation to obtain the final recommended concentration.

2. Post-production analysis is mandatory if either ethanol or an isopropanol solution is used. Use the alcoholmeter to control the alcohol concentration of the final use solution. The accepted limits should be fixed to ± 5% of the target concentration (75%–85% for ethanol).



3. The alcoholmeter shown in this information pamphlet is for use with ethanol; if used to control an isopropanol solution, a 75% solution will show 77% (± 1%) on the scale at 25°C.

General information

Labelling should be in accordance with national guidelines and should include the following:

- Name of institution
- WHO-recommended handrub formulation
- For external use only
- Avoid contact with eyes
- Keep out of the reach of children
- Date of production and batch number
- Use: Apply a palmful of alcohol-based handrub and cover all surfaces of the hands. Rub hands until dry
- Composition: ethanol or isopropanol, glycerol and hydrogen peroxide
- Flammable: keep away from flame and heat

Production and storage facilities:

- Production and storage facilities should ideally be air conditioned or cool rooms. No naked flames or smoking should be permitted in these areas.
- WHO-recommended handrub formulations should not be produced in quantities exceeding 50-litres locally or in central pharmacies lacking specialised air conditioning and ventilation.
- 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 flashpoints of ethanol 80% (v/v) and of isopropyl alcohol 75% (v/v) are 17.5°C and 19°C, respectively.
- National safety guidelines and local legal requirements must be adhered to the storage of ingredients and the final product.
- Additional safety information is presented in Part B of this Guide.

PART B: SUPPLEMENTARY TECHNICAL, SAFETY AND COST INFORMATION:

Part B contains important safety and cost information and incorporates information from the WHO Guidelines on Hand Hygiene in Health Care (2009).

The case for alcohol-based handrubs in health care

At present, alcohol-based handrubs are the only known means for rapidly and effectively inactivating a wide array of potentially harmful microorganisms on hands.

WHO recommends alcohol-based handrubs based on the following factors:

1. Evidence-based, intrinsic advantages of fast-acting and broad-spectrum microbicidal activity with a minimal risk of generating resistance to antimicrobial agents;
2. Suitability for use in resource-limited or remote areas with lack of accessibility to sinks or other facilities for hand hygiene (including clean water, towels, etc.);
3. Capacity to promote improved compliance with hand hygiene by making the process faster, more convenient and immediately accessible at the point of patient care;
4. Economic benefit by reducing annual costs for hand hygiene, representing approximately 1% of extra-costs generated by health care-associated infection
5. Minimization of risks from adverse events because of increased safety associated with better acceptability and tolerance than other products.

(Source: WHO Guidelines on Hand Hygiene in Health Care 2009)

Background to WHO alcohol-based handrub formulations

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 facilities 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 microbicidal efficacy (ASTM or EN standards) and are well accepted/tolerated by the health-care workers. It is obvious that these products should be regarded as acceptable, even if their contents differ from those of WHO-recommended formulations described within this document. WHO recommends the local production of the following formulations as an alternative when suitable commercial products are either unavailable or too costly.

To help countries and health-care facilities to achieve system change and adopt alcohol-based handrubs, WHO has identified formulations for their local preparation. Logistic, economic, safety, cultural and religious factors have all been carefully considered by WHO before recommending such formulations for use worldwide.

Efficacy

It is the consensus opinion of a WHO expert group that WHO-recommended handrub formulations can be used both for hygienic hand antisepsis and for presurgical hand preparation.

Hygienic handrub

The microbicidal activity of the two WHO-recommended formulations was tested by WHO reference laboratories according to EN standards (EN 1500). Their activity was found to be equivalent to the reference substance (isopropanol 60% v/v) for hygienic hand antisepsis.

Presurgical hand preparation

Both WHO-recommended handrub formulations were tested by two independent reference laboratories in different European countries to assess their suitability for use for pre-surgical hand preparation, according to the European Standard EN 12791. Although formulation I did not pass the test in both laboratories and formulation II in only one of them, the expert group is, nevertheless, of the opinion that the microbicidal activity of surgical antisepsis is still an ongoing issue for research as due to the lack of epidemiological data there is no indication that the efficacy of n-propanol (propan-1-ol) 60% v/v as a reference in EN 12791 finds a clinical correlate. It is the consensus opinion of a WHO expert group that the choice of n-propanol is inappropriate as the reference alcohol for the validation process because of its safety profile and the lack of evidence-based studies related to its potential harmfulness for humans. Indeed, only a few formulations worldwide have incorporated n-propanol for hand antisepsis.

Considering that other properties of WHO recommended formulations, such as their excellent tolerability, good acceptance by health-care workers and low cost are of high importance for a sustained clinical effect, the above results are considered acceptable and it is the consensus opinion of a WHO expert group that the two formulations can be used for surgical hand preparation. Institutions opting to use WHO-recommended formulations for surgical hand preparation should ensure that a minimum of three applications are used, if not more, for a period of 3–5 minutes. For surgical procedures of more than 2 hours duration, ideally surgeons should practise a second handrub of approximately 1 minute, even though more research is needed on this aspect.

Key lessons learned from around the world

Many settings around the world successfully undertook local production of the two WHO-recommended formulations. Throughout Part B, additional information is presented where relevant, in table form, based on feedback from 11 sites located in Bangladesh, Costa Rica, Egypt, Hong Kong SAR, Kenya, Mali, Mongolia, Pakistan (two sites), Saudi Arabia, and Spain. Further, detailed information is available within the WHO Guidelines on Hand Hygiene in Health Care (2009)

Composition of alcohol-based formulations for in-house/local production

The choice of components for WHO handrubs takes into account both cost constraints and microbiological efficacy. The procurement of raw ingredients will be influenced by the availability of sub-standard materials on the market and it is important to select local sources with care.

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 1

To produce final concentrations of ethanol 80% v/v, glycerol 1.45% v/v, hydrogen peroxide (H_2O_2) 0.125% v/v.

Formulation 2

To produce final concentrations of isopropyl alcohol 75% v/v, glycerol 1.45% v/v, hydrogen peroxide (H_2O_2) 0.125% v/v:

Only pharmacopoeial quality reagents should be used (e.g. The International Pharmacopoeia) and not technical grade products.

Raw materials:

While alcohol is the active component in the formulations, certain aspects of other components should be respected. All raw materials used should be preferably free of viable bacterial spores. The raw materials for inclusion/consideration are listed in the table below:

H_2O_2	• The low concentration of H_2O_2 is intended to help eliminate contaminating spores in the bulk solutions and recipients and is not an active substance for hand antisepsis. • H_2O_2 adds an important safety aspect, however the use of 3–6% for the production might be complicated by its corrosive nature and by difficult procurement in some countries. • Further investigation is needed to assess H_2O_2 availability in different countries as well as the possibility of using a stock solution with a lower concentration.
Glycerol and other humectants or emollients	• Glycerol is added as a humectant to increase the acceptability of the product. • Other humectants or emollients may be used for skin care, provided that they are affordable, available locally, miscible (mixable) in water and alcohol, non-toxic, and hypoallergenic. • Glycerol has been chosen because it is safe and relatively inexpensive. Lowering the percentage of glycerol may be considered to further reduce stickiness of the handrub.
Use of proper water	• While sterile distilled water is preferred for making the formulations, boiled and cooled tap water may also be used as long as it is free of visible particules.
Addition of other additives	• It is strongly recommended that no ingredients other than those specified here be added to the formulations. • In the case of any additions, full justification must be provided together with documented safety of the additive, its compatibility with the other ingredients, and all relevant details should be given on the product label.
Gelling agents	• No data are available to assess the suitability of adding gelling agents to WHO-recommended liquid formulations, but this could increase