TEMPORARY GUIDANCE ON REQUIREMENTS FOR ALCOHOL-BASED HAND SANITISERS

Version 1.0

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BACKGROUND

There is currently an outbreak of a respiratory disease caused by a novel coronavirus that was first detected in Wuhan City, Hubei Province, China, and has now been detected in many locations internationally including Zambia. The virus has been named "SARS-CoV-2" which stands for "Severe Acute Respiratory Syndrome-Corona Virus-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). SARS-CoV-2 has demonstrated the capability to rapidly spread, leading to significant impact on healthcare systems as well as societal disruption.

Hand hygiene is an important part of the response to COVID-19. Washing hands often with soap and water for at least 20 seconds is essential, especially after going to the bathroom, before eating, and after coughing, sneezing or blowing one's nose. The ability of hand hygiene, including hand washing or the use of alcohol-based hand sanitizers to prevent infections is related to reductions in the number of viable pathogens that transiently contaminate the hands. Hand washing mechanically removes pathogens, while the use of alcohol-based hand sanitizer containing either ethanol (not less than 60%) or 70% isopropanol (Isopropyl alcohol), as active ingredients, inactivates viruses that are genetically related to and have similar physical properties as the SARS-CoV-2.

Since the emergence of COVID-19 pandemic, the Zambia Medicines Regulatory Authority has received a number of queries concerning production or compounding of alcohol-based hand sanitizers. Hence the issuance of this guide.

NOTIFICATION TO MANUFACATURE ALCOHOL BASED HAND SANITISERS

Pursuant to the Medicines and Allied Substances Act No. 3 of 2013, the Authority is mandated to regulate allied substances such as hand sanitisers among others.

(i). A person who intends to or is undertaking the manufacture or production of hand sanitisers shall:

a) Notify the Authority in writing (to the Director-General) to express intent to manufacture the hand sanitiser
b) Furnish details such as qualifications and experience of key personnel responsible for production and quality control

(ii). Attachments to the notification letter in (i) above shall be accompanied by:

a) Sketch of the floor plan for premises
b) Certificate of business registration
c) Business levy certificate from the local authority
d) Fire certificate from the local authority
e) Any other legal requirements from relevant regulatory bodies

The Authority may inspect the premises intended for or already carrying out operations of manufacturing and quality control of hand sanitisers in order to ascertain their suitability.

COMPOSITION OF ALCOHOL-BASED FORMULATIONS FOR LOCAL PRODUCTION

In accordance with available evidence on efficacy, tolerability and cost effectiveness, WHO recommends using an alcohol-based hand sanitizer for routine hand antisepsis in most clinical situations. The following two alcohol-based hand sanitizer formulations are recommended for preparation in a local production facility:

Formulation 1To 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%$^{v}/_{v}$.

The hand sanitizer is compounded/produced using Pharmacopoeial methods (percentage in final product formulation) consistent with World Health Organization (WHO) recommendations.

Note

(i). **Glycerol**: is used as a 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 allergic reactions.

(ii). **Hydrogen peroxide**: is used to inactivate contaminating bacterial spores in the solution and is not an active substance for hand antisepsis.

(iii). Any further additives to both formulations should be clearly labelled and be non-toxic in case of accidental ingestion.

(iv). A colourant may be added to allow differentiation from other fluids, but should not add to toxicity, promote allergic reactions or interfere with the antimicrobial properties of the preparation. The addition of perfumes or dyes is not recommended due to risk of allergic reactions.

PRODUCTION AND STORAGE FACILITIES

Premises should be laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels. Below are requirements to be complied with:

(i). The part of the building used to produce hand sanitisers should have:

a) smooth, even and washable flooring which shall not retain or accumulate dust;

b) Smooth, water-proof and easy to clean walls; and

c) No chinks or crevices in the walls of floor.

(ii). Production and storage facilities should ideally be air conditioned or cool rooms;

(iii). No naked flames or smoking should be permitted in these areas;

(iv). Hand sanitizer formulations should not be produced on premises lacking specialised air conditioning and ventilation;

(v). 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;

(vi). During storage of ingredients and the final product, national safety guidelines and local legal requirements must be adhered to.

CONTAINER CLOSURE SYSTEM

All containers and closures intended for use should comply with pharmacopoeial and other specified requirements. The container closure system shall provide adequate protection against foreseeable external factors in storage/ transportation and use that may cause deterioration or contamination of the product.

LABELLING

The product label must contain a minimum of the following:

(i). Product name

(ii). Product composition stating the concentration of the active (alcohol)

(iii). Batch number

(iv). Expiry date

(v). Manufacturing date

(vi). Manufacturers name and manufacturing address

(vii). The fill volume of the container

PRODUCTION EQUIPMENT

The production space should have a minimum of 15m^2 area and below is the required equipment:

(i). Mixing tanks with stirrer (plastic-preferably in polypropylene or high-density polyethylene which is translucent so as to see the liquid level or stainless steel)

(ii). Filtering equipment (where applicable)

(iii). Filling equipment and sealing machine

(iv). Suitable measuring devices

(v). Glass or plastic bottles

(vi). Alcoholmeter

QUALITY CONTROL

Laboratory testing of manufactured batches of hand sanitizers is paramount to guarantee that the products meet set out specifications before release, for use, to the members of the public.

The following are requirements to be fulfilled:

(i). Pre-production analysis should be made every time an analysis certificate from the supplier of starting materials, especially for ethanol and isopropyl alcohol 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. These steps should be documented.

(ii). 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, that is, isopropyl alcohol 75%$^{v}/_{v}$ or ethanol 80% $^{v}/_{v.}$

(iii). The alcoholmeter 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.

(iv). The hydrogen peroxide (H_2O_2) concentration can be measured by titrimetry (oxydo-reduction reaction by iodine in acidic conditions).

(v). A higher-level quality control can be performed using gas chromatography and the titrimetric method to control the alcohol and the hydrogen peroxide content, respectively. Moreover, the absence of microbial contamination (including spores) can be checked by filtration, according to the **European Pharmacopeia specifications**.

Manufacturers who intend to prepare or compound alcohol-based hand sanitisers are advised to read these guidelines carefully and ensure compliance to the document.

ZAMRA encourages consumers and health care professionals to report adverse events experienced with the use of hand sanitizers.

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REFERENCES

(i). Itkar. S C and Vyawahare. N. S, 2015, Drug Regulatory Affairs. Nirali Prakashan, India

(ii). https://www.cdc.gov/coronavirus/2019-ncov/infection-control/hcp-hand-sanitizer.html

(iii). https://www.fda.gov/media/136118/download

https://www.who.int/gpsc/5may/Guide_to_Local_Production.pdf

GLOSSARY

The definitions provided below apply to the words and phrases used in these guidelines. Although an effort has been made to use standard definitions as far as possible, they may have different meanings in other contexts and documents.

Alcoholmeter means an instrument used to determine the strength of spirits, with a scale graduated so as to indicate the percentage of pure alcohol.

Antisepsis means the prevention of infection by inhibiting the growth and multiplication of germs (infectious agents).

Batch means a defined quantity of medicines and allied substances processed in a single process or series of processes so that it is expected to be homogeneous.

Batch number means a distinctive combination of numbers or letters which uniquely identifies a batch.

Container Closure System means packaging components that together contain and protect the product. This includes primary packaging components and secondary packaging components.

Emollient means a moisturising treatment applied directly to the skin to soothe and hydrate it.

Epidemic means the rapid spread of disease to a large number of people in a given population within a short period of time.

Flash Point means the lowest temperature at which a liquid will form a vapour in the air near its surface that will “flash,” or briefly ignite, on exposure to an open flame. The flash point is a general indication of the flammability or combustibility of a liquid,

Humectant means a substance that promotes retention of moisture.

Labelling means a process of identifying a product and includes the following

information, as appropriate: name of the product; active ingredient(s), type and amount; batch number; expiry date; special storage conditions or handling precautions; directions for use, warnings and precautions; names and addresses of the manufacturer or the supplier.

Manufacture means all operations of purchase of materials and products, production, quality control (QC), release, storage and distribution of pharmaceutical products, and the related controls.

Pandemic means a disease that has spread across a large region, for instance multiple continents, or worldwide at the same time.

Pharmacopoeia means a book describing drugs, chemicals and medicinal preparations especially on issued by an officially recognised authority and serving as a standard.

Production means all operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.

SARS-CoV-2 means Severe Acute Respiratory Syndrome-Corona Virus-2.

Quality Control means all measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

WHO means World Health Organisation, a specialised agency of the United Nations responsible for international public health.