Production of isopropyl alcohol for use in alcohol-based hand sanitizers: interim guide

This interim guide contains information on isopropyl alcohol in alcohol-based hand sanitizers. Guidance on quality requirements and formulations is also provided.

On this page

This document provides information on the use of isopropyl alcohol (IPA) as the medicinal ingredient in alcohol-based hand sanitizers sold in Canada. Numerous entities and industries that are not currently regulated by Health Canada have expressed interest in providing additional and/or alternate sources of alcohol for use in the production of hand sanitizers to support the national response to the supply shortage during the COVID-19 pandemic.

Please also refer to the Guide on Health Canada's Interim Expedited Licensing Approach for the Production and Distribution of Alcohol-Based Hand Sanitizers, which Health Canada launched on March 27, 2020. The Guide has useful information on the authorizations required to manufacture, package, label and/or distribute alcohol-based hand sanitizers, including information on the simplified and expedited pathway to obtaining the required authorizations (a product licence and/or a site licence) in the context of the COVID-19 response.

This document provides further guidance on the quality requirements for IPA used in the production of hand sanitizers. It also highlights acceptable formulations and considerations for parties interested in manufacturing IPA-based hand sanitizers during this emergency situation.

To protect the health and safety of Canadians, Health Canada remains committed to its mandate while balancing the need for exceptional measures during the COVID-19 pandemic. The quality of IPA used in manufacturing hand sanitizers must be fit for purpose and meet safety, efficacy and quality requirements in the *Natural Health Products Regulations* (NHPR).

This interim approach takes into account the current policies and best practices of foreign regulatory partners as well as recommendations of the World Health Organization (WHO).

Acceptable quality grades

IPA used for the production of hand sanitizers must conform to one of the identity and purity criteria published in any of the following quality standards, with any acceptable deviations found within those standards. For details on these quality standards, please refer to the weblinks provided below. Please note that some of these references may be accessed for free, while others require payment for full access:

- U.S. Pharmacopeia (USP)
- European Pharmacopeia (Ph. Eur.)
- Food Chemical Codex (FCC)
- British Pharmacopoeia (BP)
- Pharmacopée française (Ph.f.) (in french only)
- Pharmacopoeia Internationalis (Ph.I.)
- Japanese Pharmacopoeia (JP)
- National Formulary (NF)

Testing must follow the methodology for the IPA outlined in the reference you are using to be considered to meet the acceptable quality standard.

Unacceptable grades

Laboratory/electronic grade IPA is typically used for educational purposes or electronic equipment cleaning, however the exact identity and quantity of impurities are unknown, especially with respect to those that may be introduced through the manufacturing process. These impurities are potentially undetected by food or drug analysis methods suited for human application. As such, laboratory/electronic grade IPA is not acceptable for use in hand sanitizer production or importation in Canada.

Technical grade

Technical grade IPA is a broad term encompassing various purity and contaminant profiles. Only IPA that meets one of the above acceptable quality grades, is manufactured for human use as a food or drug, and has no other impurities outside of the limits established in the acceptable quality standards (including non-volatile residue introduced through the manufacturing process) is acceptable for use in hand sanitizers.

The following are two additional examples of technical grades of IPA that are not typically used in pharmaceuticals but may also meet or exceed Health Canada's quality expectations:

- **American Chemical Society (ACS) grade**: This grade is acceptable for food, drug, or medicinal use and can be used for ACS applications or for general procedures that require stringent quality specifications and a purity of ≥ 95%

- **Reagent grade**: This grade is generally equal to ACS grade (≥95%) and is acceptable for food, drug, or medicinal use and is suitable for use in many laboratory and analytical applications

For ACS and Reagent grades, companies are required to undertake additional testing to identify and account for the totality of impurities found in the IPA. These tests, and the acceptable methodologies, are outlined in the USP monograph for IPA. This includes:

- identification testing (infrared absorption)
- quantification testing (gas chromatography)
- impurities testing (identity and quantity) for volatile impurities and non-volatile residues
- testing that provides information on the gravity, refractive index, acidity and water determination to determine if, or how far away, the product is from meeting acceptable quality standards

You must ensure that:

- the testing methods are those outlined in the USP monograph to determine if the product is of acceptable quality
- the total % of impurities does not exceed levels set out in the acceptable quality grades
- no single impurity exceeds established thresholds in the acceptable quality standards
- quality controls are in place to ensure that there has been no mixing or contamination of the IPA

It is important that any technical grade product used must be consistent with the type of raw material that would be typically used for food or drugs, and no other additives or other chemicals have been added to the IPA. Further, special caution should be taken to ensure any other chemicals on site are not introduced into the IPA either intentionally or via cross contamination. Because of the potential for the presence of potentially harmful impurities due to the processing approach, it is paramount that any technical grade IPA should only be used if it meets the above reference grade requirements. If this has not been done, your IPA cannot be considered fit for human use and acceptable for use as a raw material in hand sanitizer.

You must always have a product licence, signified by an NPN to manufacture, distribute, or import alcohol based hand sanitizer. This product licence does not specify the type of IPA you are permitted to use. If you plan to use technical grade IPA in your hand sanitizer, you must notify Health Canada **before** you start using it, even if you already have a product licence. This notification will allow Health Canada to contact you when this interim approach allowing technical grade IPA to be used in hand sanitizer ends.

To notify Health Canada that you will be using technical grade IPA in your hand sanitizer, email the Natural and Non-prescription Health Products Directorate at

hc.rmd.coordination-dgr.sc@canada.ca with the following subject line **COVID-19 – Notification of technical grade IPA use in hand sanitizer**. This notification must include:

- name of company
- whether you have a product licence and/or a site license
    - if so, your product number or site number
- a statement attesting to meeting the requirements established above (including that the IPA meets, is the equivalent of or exceeds an acceptable quality grade listed above)

Once you have submitted your notification, you do not need to wait for a response from Health Canada before manufacturing, distributing, or importing the product using technical grade IPA, provided that you have a been issued a product licence.

If you cannot make the attestation as your IPA does not meet the appropriate quality grades listed above, your IPA would not be considered acceptable for use as a raw ingredient in hand sanitizer.

Note: It is the responsibility of the product license holder to verify compliance of raw material with any and all requirements, such as those that relate to the appropriate testing and qualifications of technical grade IPA.

Recommended formulation

All formulations must meet the safety and efficacy requirements established in Health Canada's Antiseptic Skin Cleansers (Personal Domestic Use) monograph.

Health Canada recommends that IPA-based hand sanitizers be manufactured according to the WHO formulation below. This formulation ensures that impurities commonly found in IPA should not exceed USP limits.

Formulation for a 10-litre preparation

- Isopropyl alcohol 99.8% : 7515 ml
- Hydrogen peroxide 3% : 417 ml

- Glycerol 98% : 145 ml
- Water: Up to 10L

The final preparation contains 75% IPA, 0.125% hydrogen peroxide, 1.421% glycerol, and water.

Other acceptable formulations, which result in final preparations with the same ratios, include:

- the USP guidance, as updated on March 25, 2020
- the US FDA guidance, released on March 27, 2020

Records

Records must be maintained on how the hand sanitizer is prepared, including details on how the final IPA dilution in the finished product was derived. The amount of IPA needed in the formulation should be calculated using the following equation (as set out in the USP guidance):

$$\frac{\text{(final \% alcohol)} \times \text{(final volume of preparation)}}{\text{(starting \% alcohol)}} = \text{volume of starting ingredient required}$$

Long description

The volume of starting ingredient required is calculated by multiplying the final percentage of alcohol by the final volume of preparation, and then dividing by the starting percentage of alcohol.

Documentation including certificates of analysis (CoA) must be kept on record and made available at the request of Health Canada.

Non-medicinal ingredients

All non-medicinal ingredients (NMIs) used in a hand sanitizer product must be listed in Health Canada's Natural Health Products Ingredient Database (NHPID) and comply with all listed restrictions (as per the NHPID).

While non-sterile water can be used in place of sterile water, you should ensure that the water system is being continuously monitored, for example by monitoring bacterial counts to ensure they are within acceptable ranges for IPA (see applicable good manufacturing guidance for additional information on microbial testing). This may necessitate additional precautions in relation to contamination. If non-sterile water is

used, additional testing is also required to ensure quality of the finished product prior to distribution (for instance, sale or donation).

Any substitutions must be ingredients identified in the NHPID and you must notify Health Canada of such a change (no response from Health Canada is required). If the NMI that you intend to use is not found in the NHPID, you may complete a Natural Health Products Ingredients Database Issue Form and submit to ingredient_support@hc-sc-gc.ca to ask to have the ingredient added.

Manufacturer responsibilities of the finished dosage

In addition to the responsibilities of the raw material supplier in following good manufacturing practices, the good manufacturing practices listed in the NHPR must be applied for all finished dosage form NHPs, including hand sanitizers. For instance, the quality assurance person/department must maintain the following:

- you are responsible to confirm that the isopropyl alcohol lot you have purchased/acquired includes a lab report with impurities results listed that then must be compared to the USP acceptable limits
- you must be able to trace each lot of isopropyl alcohol to the products you have produced
- you must be able to effectively recall your product in the event that a quality issue arises
- you must quarantine any suspect lots of isopropyl alcohol or finished hand sanitizers and take steps to ensure that quarantined product is not released for use or sale

Labelling requirements

You must meet the labelling requirements outlined in the Guide on Health Canada's Interim Expedited Licensing Approach for the Production and Distribution of Alcohol-Based Hand Sanitizers. There are no specific, additional labelling requirements for hand sanitizers containing IPA as any IPA (including technical grade) acceptable for use in hand sanitizers needs to meet or exceed the quality standards set out in this guide.

Excise tax implications

Alcohol importers may have additional registration requirements under legislative frameworks, such as *Excise Act,* 2001, which is administered by the Canada Revenue Agency (CRA). It is your responsibility to check with any other licensing bodies, such as the CRA, to understand the implications of your formulation on any authorizations producing and using alcohol.

For questions or further information, please visit this website Excise Duties, Excise Taxes, Fuel Charge and Air Travellers Security Charge, which also includes the contact information for your regional excise duty office. These regional offices are your best source for information on excise taxes.

End of interim approach

Health Canada will lift the interim measure when the regular supply stabilizes.

Contact us

If you have questions regarding the use of technical grade IPA, you can contact Health Canada's Natural and Non-prescription Health Products Directorate at hc.nnhpd-dpsnso.sc@canada.ca.