Isopropyl Alcohol

1 Nonproprietary Names
BP: Isopropyl Alcohol
JP: Isopropanol
PhEur: Isopropyl Alcohol
USP: Isopropyl Alcohol

2 Synonyms
Alcohol isopropylicus; dimethyl carbinol; IPA; isopropanol; petrolhol; 2-propanol; sec-propyl alcohol; rubbing alcohol.

3 Chemical Name and CAS Registry Number
Propan-2-ol [67-63-0]

4 Empirical Formula and Molecular Weight
C₃H₈O 60.1

5 Structural Formula

6 Functional Category
Disinfectant; solvent.

7 Applications in Pharmaceutical Formulation or Technology
Isopropyl alcohol (propan-2-ol) is used in cosmetics and pharmaceutical formulations, primarily as a solvent in topical formulations. It is not recommended for oral use owing to its toxicity; see Section 14.

Although it is used in lotions, the marked degreasing properties of isopropyl alcohol may limit its usefulness in preparations used repeatedly. Isopropyl alcohol is also used as a solvent both for tablet film-coating and for tablet granulation, where the isopropyl alcohol is subsequently removed by evaporation. It has also been shown to significantly increase the skin permeability of nimesulide from carbomer 934. Isopropyl alcohol has some antimicrobial activity and a 70% v/v aqueous solution is used as a topical disinfectant. Therapeutically, isopropyl alcohol has been investigated for the treatment of postoperative nausea or vomiting.

8 Description
Isopropyl alcohol is a clear, colorless, mobile, volatile, flammable liquid with a characteristic, spirituous odor resembling that of a mixture of ethanol and acetone; it has a slightly bitter taste.

9 Pharmacopeial Specifications
See Table I.

<table>
<thead>
<tr>
<th>Test</th>
<th>JP XV</th>
<th>PhEur 6.0</th>
<th>USP 32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Appearance of solution</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Absorbance</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Characters</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>0.785–0.788</td>
<td>0.785–0.789</td>
<td>0.783–0.787</td>
</tr>
<tr>
<td>Refractive index</td>
<td>—</td>
<td>1.376–1.379</td>
<td>1.376–1.378</td>
</tr>
<tr>
<td>Acidity or alkalinity</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Water</td>
<td>≤0.75%</td>
<td>≤0.5%</td>
<td>—</td>
</tr>
<tr>
<td>Nonvolatile residue</td>
<td>≤1.0 mg</td>
<td>≤20 ppm</td>
<td>≤0.005%</td>
</tr>
<tr>
<td>Distillation range</td>
<td>81–83 °C</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Benzene</td>
<td>—</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>Peroxides</td>
<td>—</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>Assay</td>
<td>—</td>
<td>—</td>
<td>≥99.0%</td>
</tr>
</tbody>
</table>

10 Typical Properties

Antimicrobial activity: Isopropyl alcohol is bactericidal; at concentrations greater than 70% v/v it is a more effective antibacterial preservative than ethanol (95%). The bactericidal effect of aqueous solutions increases steadily as the concentration approaches 100% v/v. Isopropyl alcohol is ineffective against bacterial spores.

Autoignition temperature 425°C
Boiling point 82.4°C
Dielectric constant $D_{20}^2 = 18.62$
Explosive limits 2.5–12.0% v/v in air
Flammability Flammable.
Flash point 11.7°C (closed cup); 13°C (open cup). The water azeotrope has a flash point of 16°C.
Freezing point –89.5°C
Melting point –88.5°C
Moisture content 0.1–13% w/w for commercial grades (13% w/w corresponds to the water azeotrope).
Refractive index
$n_{D}^{20} = 1.3776$
$n_{D}^{25} = 1.3749$
Solubility Miscible with benzene, chloroform, ethanol (95%), ether, glycerin, and water. Soluble in acetone; insoluble in salt.
Isopropyl alcohol should be stored in an airtight container in a cool, dry place.

12 Incompatibilities
Incompatible with oxidizing agents such as hydrogen peroxide and nitric acid, which cause decomposition. Isopropyl alcohol may be salted out from aqueous mixtures by the addition of sodium chloride, sodium sulfate, and other salts, or by the addition of sodium hydroxide.

13 Method of Manufacture
Isopropyl alcohol may be prepared from propylene; by the catalytic reduction of acetone, or by fermentation of certain carbohydrates.

14 Safety
Isopropyl alcohol is widely used in cosmetics and topical pharmaceutical formulations. It is readily absorbed from the gastrointestinal tract and may be slowly absorbed through intact skin. Prolonged direct exposure of isopropyl alcohol to the skin may result in cardiac and neurological deficits.\(^5\) In neonates, isopropyl alcohol has been reported to cause chemical burns following topical application.\(^6,7\)

Isopropyl alcohol is metabolized more slowly than ethanol, primarily to acetone. Metabolites and unchanged isopropyl alcohol are mainly excreted in the urine.

Isopropyl alcohol is about twice as toxic as ethanol and should therefore not be administered orally; isopropyl alcohol also has an unpleasant taste. Symptoms of isopropyl alcohol toxicity are similar to those for ethanol except that isopropyl alcohol has no initial euphoric action, and gastritis and vomiting are more prominent; see Alcohol. Delta osmolality may be useful as rapid screen test to identify patients at risk of complications from ingestion of isopropyl alcohol.\(^8\) The lethal oral dose is estimated to be about 120–250 mL although toxic symptoms may be produced by 20 mL.

Adverse effects following parenteral administration of up to 20 mL of isopropyl alcohol diluted with water have included only a sensation of heat and a slight lowering of blood pressure. However, isopropyl alcohol is not commonly used in parenteral products.

Although inhalation can cause irritation and coma, the inhalation of isopropyl alcohol has been investigated in therapeutic applications.\(^9\)

Isopropyl alcohol is most frequently used in topical pharmaceutical formulations where it may act as a local irritant.\(^10\) When applied to the eye it can cause corneal burns and eye damage.

LD\(_{50}\) (dog, oral): 4.80 g/kg\(^9\)
LD\(_{50}\) (mouse, oral): 3.6 g/kg
LD\(_{50}\) (mouse, IP): 4.48 g/kg
LD\(_{50}\) (mouse, IV): 1.51 g/kg
LD\(_{50}\) (rabbit, oral): 6.41 g/kg
LD\(_{50}\) (rabbit, skin): 12.8 g/kg
LD\(_{50}\) (rat, IP): 2.74 g/kg

LD\(_{50}\) (rat, IV): 1.09 g/kg
LD\(_{50}\) (rat, oral): 5.05 g/kg

15 Handling Precautions
Observe normal precautions appropriate to the circumstances and quantity of material handled. Isopropyl alcohol may be irritating to the skin, eyes, and mucous membranes upon inhalation. Eye protection and gloves are recommended. Isopropyl alcohol should be handled in a well-ventilated environment. In the UK, the long-term (8-hour TWA) workplace exposure limit for isopropyl alcohol is 999 mg/m\(^3\) (400 ppm); the short-term (15-minute) workplace exposure limit is 1250 mg/m\(^3\) (500 ppm).\(^10\) OSHA standards state that IPA 8-hour time weighted average airborne level in the workplace cannot exceed 400 ppm. Isopropyl alcohol is flammable and produces toxic fumes on combustion.

16 Regulatory Status
Included in the FDA Inactive Ingredients Database (oral capsules, tablets, and topical preparations). Included in nonparenteral medicines licensed in the UK. Included in the Canadian List of Acceptable Non-medicinal Ingredients.

17 Related Substances
Propan-1-ol.

Propan-1-ol
Empirical formula C\(_3\)H\(_8\)O
Molecular weight 60.1
CAS number [71-23-8]
Synonyms Propanol; n-propanol; propyl alcohol; propyl alcohol.
Autoignition temperature 540°C
Boiling point 97.2°C
Dielectric constant D\(_{25}\) = 22.20
 Explosive limits 2.15–13.15% v/v in air
Flash point 15°C (closed cup)
Melt point –12°C
Refractive index n\(_{D20}\) = 1.3862
Solubility Miscible with ethanol (95%), ether, and water.
Specific gravity 0.8053 at 20°C
Viscosity (dynamic) 2.3 mPa s (2.3 cP) at 20°C

18 Comments
A specification for isopropyl alcohol is contained in the Food Chemicals Codex (FCC).\(^11\)

The EINECS number for isopropyl alcohol is 200-661-7. The PubChem Compound ID (CID) for isopropyl alcohol is 3776.

19 Specific References
Isopropyl Myristate

1 Nonproprietary Names
BP: Isopropyl Myristate
PhEur: Isopropyl Myristate
USP-NF: Isopropyl Myristate

2 Synonyms
Estol IPM; HallStar IPM-NF; isopropyl ester of myristic acid; Isopropylmyristat; isopropylis myristas; Kessco IPM 95; Lexol IPM-NF; myristic acid isopropyl ester; Rita IPM; Stepan IPM; Super Refined Crodamol IPM; Tegosoft M; tetradecanoic acid, 1-methylethyl ester; Waglinol 6014.

3 Chemical Name and CAS Registry Number
1-Methylethyl tetradecanoate [110-27-0]

4 Empirical Formula and Molecular Weight
C_{17}H_{34}O_{2}    270.5

5 Structural Formula

6 Functional Category
Emollient; oleaginous vehicle; skin penetrant; solvent.

7 Applications in Pharmaceutical Formulation or Technology
Isopropyl myristate is a nongreasy emollient that is absorbed readily by the skin. It is used as a component of semisolid bases and as a solvent for many substances applied topically. Applications in topical pharmaceutical and cosmetic formulations include bath oils; make-up; hair and nail care products; creams; lotions; lip products; shaving products; skin lubricants; deodorants; otic suspensions; and vaginal creams; see Table I. For example, isopropyl myristate is a self-emulsifying component of a proposed cold cream formula, which is suitable for use as a vehicle for drugs or dermatological actives; it is also used cosmetically in stable mixtures of water and glycerol. Isopropyl myristate is used as a penetration enhancer for transdermal formulations, and has been used in conjunction with therapeutic ultrasound and iontophoresis. It has been used in a water-oil gel prolonged-release emulsion and in various microemulsions. Such microemulsions may increase bioavailability in topical and transdermal applications. Isopropyl myristate has also been used in microspheres, and significantly increased the release of drug from eutopside-loaded microspheres. Isopropyl myristate is used in soft adhesives for pressure-sensitive adhesive tapes.

Table I: Uses of isopropyl myristate.

<table>
<thead>
<tr>
<th>Use</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detergent</td>
<td>0.003–0.03</td>
</tr>
<tr>
<td>Otic suspension</td>
<td>0.024</td>
</tr>
<tr>
<td>Perfumes</td>
<td>0.5–2.0</td>
</tr>
<tr>
<td>Microemulsions</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Soap</td>
<td>0.03–0.3</td>
</tr>
<tr>
<td>Topical aerosols</td>
<td>2.0–98.0</td>
</tr>
<tr>
<td>Topical creams and lotions</td>
<td>1.0–10.0</td>
</tr>
</tbody>
</table>

8 Description
Isopropyl myristate is a clear, colorless, practically odorless liquid of low viscosity that congeals at about 5°C. It consists of esters of propan-2-ol and saturated high molecular weight fatty acids, principally myristic acid.

9 Pharmacopeial Specifications
See Table II.

10 Typical Properties
Boiling point        140.2°C at 266 Pa (2 mmHg)
Flash point          153.5°C (closed cup)
Freezing point       ≈5°C
Solubility           Soluble in acetone, chloroform, ethanol (95%), ethyl acetate, fats, fatty alcohols, fixed oils, liquid hydrocarbons, toluene, and waxes. Dissolves many waxes, cholesterol, or lanolin. Practically insoluble in glycerin, glycols, and water.
Viscosity (dynamic)  5–7 mPa s (5–7 cP) at 25°C