Ensuring Quality Hand Sanitizer Production During COVID-19 Seminar

Formulating Quality Alcohol-Based Hand Sanitizer

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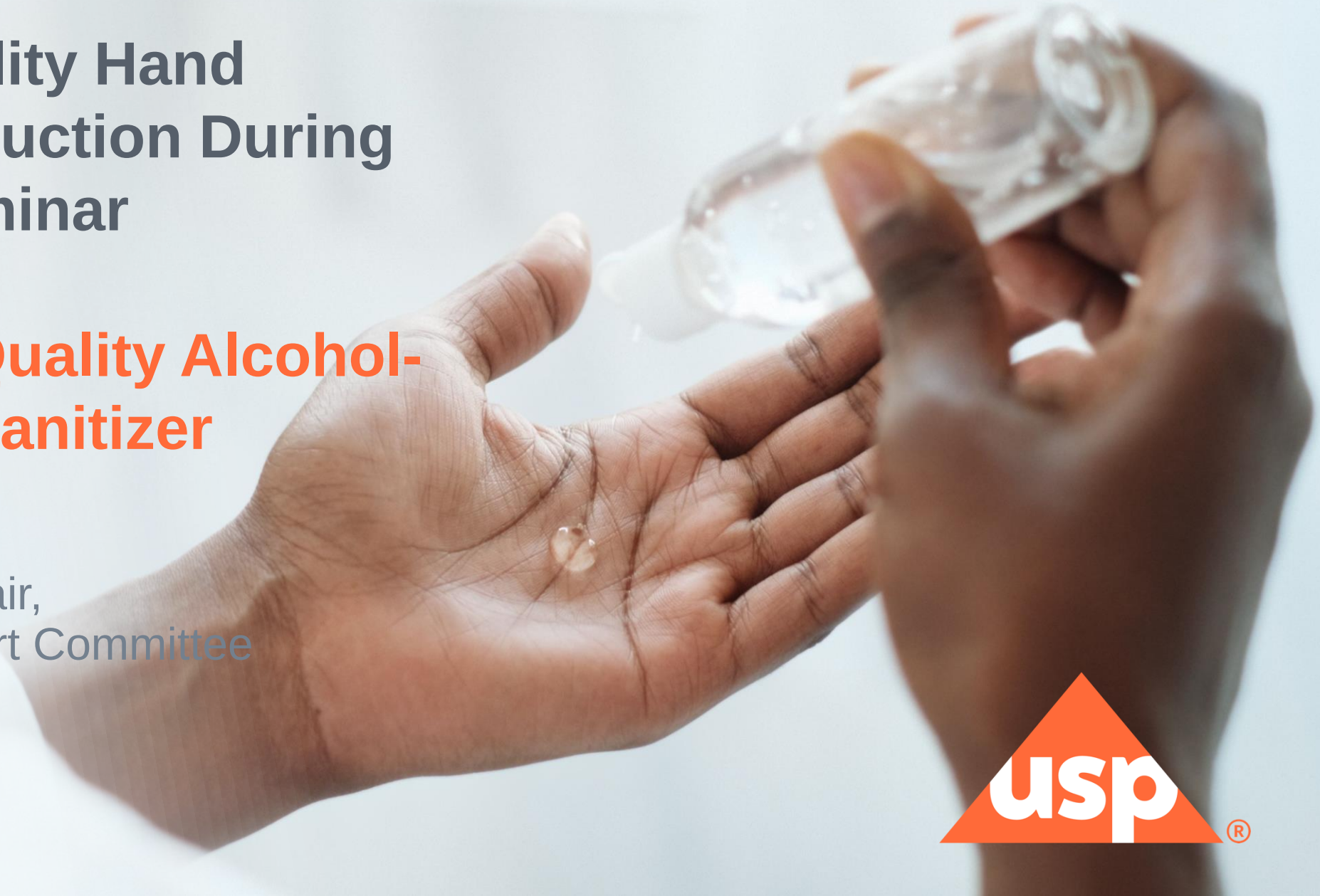

Agenda

1. Responsibilities of the Compounder
2. Formulating Quality Alcohol-Based Hand Sanitizer
3. Quality Control and Quality Assurance

Responsibilities of the Compounder

- The compounder must be proficient in compounding
- The compounder must prepare compounded nonsterile preparations:
  - with acceptable strength, quality, and purity
  - with appropriate packaging and labeling
  - in compliance with established state agencies, state boards of pharmacy, federal law, and other regulatory agencies

Formulating Quality Alcohol-Based Hand Sanitizer

Formulation 1

- **Ethanol** [1,2] **96%** 8333 mL
- **Hydrogen peroxide 3%** 417 mL
- **Glycerol** [3] **98%** 145 mL
- **Water** [4] **sufficient quantity to make** 10,000 mL

Formulation 2

- **Isopropyl Alcohol** [1] **99%** 7576 mL
- **Hydrogen peroxide 3%** 417 mL
- **Glycerol** [3] **98%** 75 mL
- **Water** [4] **a sufficient quantity to make** 10,000 mL

Formulation 3

- **Isopropyl Alcohol** [1] **91%** 8242 mL
- **Hydrogen peroxide 3%** 417 mL
- **Glycerol** [3] **98%** 75 mL
- **Water** [4] **a sufficient quantity to make** 10,000 mL

[1] When the concentration of alcohol in the starting ingredient is not exact, follow the calculation on the USP hand sanitizer resource document to ensure a final concentration of at least 80% ethanol or 75% isopropyl alcohol.

[2] It is recommended to use denatured ethanol instead of nondenatured ethanol because there have been reports of adverse events, including deaths, from unintentional ingestion of hand sanitizer, particularly in young children. If it is not denatured, package in a child-resistant container.

[3] Glycerin and glycerol are synonymous and may be interchanged. Glycerin and glycerol are added as humectants.

[4] Water may be distilled, cold boiled potable, reverse osmosis, or filtered.

Packaging and Storage: Package in well-closed, suitable containers and store at controlled room temperature.

Labeling: Label it to state for external use only, the percentage of active ingredient (i.e., ethanol, isopropyl alcohol), and the *Beyond-Use Date*.

Beyond-Use Date: NMT 30 days after the date on which it was compounded when stored at controlled room temperature.

Formulating Quality Alcohol-Based Hand Sanitizer

- Ingredients
  - USP, NF, or Food Chemicals Codex (FCC) grade ingredients should be used as the recommended source of ingredients
  - First attempt from FDA-registered facility
  - If ingredients from a non-FDA registered facility are required, use professional judgment (e.g., Certificate of Analysis, manufacturer reputation, reliability of source)

Formulating Quality Alcohol-Based Hand Sanitizer

- Ingredients for 10,000 mL
  - Ethanol 96% 8333 mL or
    - If Ethanol is used, denaturing is recommended
  - Isopropyl Alcohol 99% 7576 mL or
  - Isopropyl Alcohol 91% 8242 mL

Formulating Quality Alcohol-Based Hand Sanitizer

- When the concentration of alcohol (e.g., ethanol or isopropyl alcohol) in the starting ingredient is not exact, the calculation should be adjusted accordingly to ensure a final concentration of at least 80% ethanol or 75% isopropyl alcohol
- Volume of starting ingredient required =

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

Formulating Quality Alcohol-Based Hand Sanitizer

- Methanol contamination of Alcohol
  - Serious safety concern
  - Substantial methanol exposure can result in nausea, vomiting, headache, blurred vision, permanent blindness, seizures, coma, permanent damage to the nervous system or death
  - Methanol must not be used as an ingredient or as a denaturant
  - Methanol content must not exceed 630 ppm[1]

[1]Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Immediately in Effect Guidance for Industry Updated February 10, 2021

Formulating Quality Alcohol-Based Hand Sanitizer

- Impurity Interim Limit under Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency Immediately in Effect Guidance for Industry Updated February 10, 2021
  - Methanol NMT 630 ppm
  - Benzene NMT 2 ppm
  - Acetaldehyde NMT 50 ppm*
  - Acetal (1,1-diethoxyethane) NMT 50 ppm
  - Sum of all other impurities NMT 300 ppm

Formulating Quality Alcohol-Based Hand Sanitizer

Table A: Preferred formula for denaturing ethanol based on 27 CFR 21.76 Formula 40-B

27 CFR 21.76 Formula No. 40-B	Conversion to metric units
To every 100 gallons of alcohol add: • One-sixteenth avoirdupois ounce of denatonium benzoate, N.F. and 1/8 gallon of tert-butyl alcohol OR To every 100 gallons of alcohol add: • One-sixteenth avoirdupois ounce of denatonium benzoate, N.F.	For 10 L of ethanol add: • 0.0468 g of denatonium benzoate, N.F., and • 12.5 mL of tert-butyl alcohol* OR For 10 L of ethanol add: • 0.0468 g of denatonium benzoate, N.F.

Formulating Quality Alcohol-Based Hand Sanitizer

Table B: Alternative Formula for denaturing ethanol based on 27 CFR 21.75 Formula 40-A

27 CFR 21.75 Formula No. 40-A	Conversion to metric units
To every 100 gallons of alcohol add: • One pound of sucrose octaacetate and 1/8 gallon of tert-butyl alcohol OR To every 100 gallons of alcohol add: • One pound of sucrose octaacetate	For 10 L of ethanol add: • 11.98 g of sucrose octaacetate • 12.5 mL of tert-butyl alcohol OR For 10 L of ethanol add: • 11.98 g of sucrose octaacetate

Table C: Alternative Formula for denaturing ethanol based on 27 CFR 21.37 Formula 3-C

27 CFR 21.37 Formula No. 3-C	Conversion to metric units
To every 100 gallons of alcohol add: • Five gallons of isopropyl alcohol	For 10 L of ethanol add: • 500 mL of isopropyl alcohol

Formulating Quality Alcohol-Based Hand Sanitizer

- Ingredients
  - Hydrogen Peroxide 3%
  - Glycerol (or Glycerin) 98%
  - Water

Formulating
Quality Alcohol-Based Hand Sanitizer

Glycerol; Glycerin; 56-81-5; Glycerine; 1,2,3-Propanetriol; PROPANE-1,2,3-TRIOL; Glycyl Alcohol; Trihydroxypropane; ...

Compound CID: 753

MF: $C_3H_8O_3$ **MW:** 92.09g/mol

InChIKey: PEDCQBHIVMGVHV-UHFFFAOYSA-N

IUPAC Name: propane-1,2,3-triol

Create Date: 2004-09-16

https://pubchem.ncbi.nlm.nih.gov/#query=glycerol accessed 2-15-21

Formulating Quality Alcohol-Based Hand Sanitizer

- *Purified Water* or
  - Distilled water
  - Cold boiled potable water
  - Reverse osmosis water
  - Filtered water

Formulating Quality Alcohol-Based Hand Sanitizer

- Measure the quantities of Ethanol or Isopropyl Alcohol, Hydrogen Peroxide, and Glycerol in suitable containers
- Transfer the Ethanol or Isopropyl Alcohol and Hydrogen Peroxide into a suitable calibrated container and mix gently
- Transfer the Glycerol stepwise and quantitatively into the calibrated container
- Mix gently after each addition
- Rinse the container containing glycerol several times with Water and add the contents to the calibrated container
- Add sufficient Water to bring to final volume
- Mix well
- Transfer the solution into suitable containers

Formulating Quality Alcohol-Based Hand Sanitizer

- Packaging and Storage
  - Package in well-closed, suitable containers and store at controlled room temperature
- Labeling
  - Label to state for external use only, the percentage of Ethanol or Isopropyl Alcohol, and the Beyond-Use Date
- ` Beyond-Use Date
  - NMT 30 days after the date on which it was compounded, when stored at controlled room temperature

Quality Control and Quality Assurance

- Policies and Procedures
  - Facility
  - Compounding Personnel
  - Selection of Ingredients
  - Equipment
  - Compounding Process
  - Quality Control
  - Error Prevention, Quality-Related Events and Adverse Reactions

Quality Control and Quality Assurance

- Facility
  - Adequate space
  - Clean, orderly, sanitary, and in a good state of repair
  - Orderly placement of equipment and materials
  - Designed, arranged, and used to prevent cross-contamination
  - Well-lighted
  - Appropriate heating, ventilation and air conditioning
  - Hand and equipment washing facilities

Quality Control and Quality Assurance

- Compounding Personnel need documented training and competency including:
  - Facility Policies and Procedures
  - *USP* <795> *Pharmaceutical Compounding – Nonsterile Preparations*
  - Equipment selection, use, cleaning, calibration, and maintenance
  - Compounding process and release checks
  - Spill clean up and Safety Data Sheets
  - Waste segregation and removal
  - Documentation requirements

Quality Control and Quality Assurance

- Selection of Ingredients
  - USP, NF, or Food Chemicals Codex (FCC) grade ingredients should be used as the recommended source of ingredients
  - First attempt from FDA-registered facility
  - If ingredients from a non-FDA registered facility are required, use professional judgment (e.g., Certificate of Analysis, manufacturer reputation, reliability of source)

Quality Control and Quality Assurance

- Equipment
  - Appropriate for use
  - Used appropriately
  - Clean
  - Calibrated
  - Maintained

Quality Control and Quality Assurance

- Compounding Process
  - Master Formulation Record
  - Compounding Record
- Quality Control
  - In-process Checks
  - Release Checks
- Quality Assurance
  - Error Prevention
  - Adverse Events

Need More Information?

CompoundingSL@usp.org

Thank You

Empowering a healthy tomorrow