

USP Seminar: Ensuring Quality Hand Sanitizer Production During COVID-19 for Manufacturers in India

Executive Summary

Alcohol-based hand sanitizer is an important element in infection prevention, especially during the COVID-19 pandemic. However, when quality is compromised, it can be less effective against infection transmission and can also lead to user harm.

COVID-19-related supply chain pressures have created global shortages that led to new vendors, materials, and production pathways to meet demand. These fast-paced changes have caused an emergence of quality incidents both regionally and globally. Globally, over 200 alcohol-based hand sanitizer quality incidents have been reported in 2020ⁱ. Specifically, there were 21 reported cases of hand sanitizer quality incidents in Indiaⁱⁱ.

To help ensure quality alcohol-based hand sanitizer production and support the safe use of alcohol-based hand sanitizer, USP hosted a day-long seminar for manufacturers in India. Around 40 individuals registered to participate in USP's Seminar on February 25, 2021, including manufacturers who produce alcohol-based hand sanitizer, representatives from regulatory agencies, and others from interested industry groups.

Presenters from USP, Government of the National Capital Territory's Drugs Control Department, Government of Gujarat's Department of Health and Family Welfare, Consumer Guidance Society of India, U.S. Food and Drug Administration (FDA) and Perrigo discussed the global and regional quality risks and solutions when producing alcohol-based hand sanitizer.

The following are key takeaways from the presentations and responses to the questions posed by participants during the seminar.

Key Takeaways

Quality Challenges and Public Health Impact

- When producing alcohol-based hand sanitizers, there are potential quality risks to the product and its ingredients, including contamination.
- An alcohol-based hand sanitizer product can be subpotent, meaning it has less than the required amount of an alcohol-based ingredient.
- If quality specifications for alcohol-based hand sanitizer products and its ingredients are not met, contamination or impurities could be introduced. Additionally, quality specifications help ensure the correct potency, so the product is not subpotent or super-potent.
- Globally, over 200 alcohol-based quality incidents have been reported in 2020ⁱⁱⁱ, with approximately 21 incidents in India^{iv}.
- In India, the sudden demand for hand sanitizers during COVID-19 led to anybody who asked for a license receiving one, which led to a lack of quality control.
 - Initially, sub-standard products (some not even containing alcohol) and herbal products hit the market.
 - Then prices skyrocketed as demand outstripped supply.
 - The Essential Commodities Act was invoked to bring the cost down to Rs. 50 for 100ml.



- In the United States, one batch of contaminated alcohol-based hand sanitizer caused 15 cases of hospitalized methanol poisoning, which led to four patient deaths and three with visual impairments^v.
 - Alcohol-based hand sanitizers that are contaminated with methanol can cause brain and ocular toxicity, metabolic acidosis, and stroke. Many of the cases seen in hospitals are intentional misuse of alcohol-based hand sanitizer, as a cheaper and more accessible alternative to alcohol. Most people are not aware of the potential for methanol contamination when misusing.
- Proper labeling and packaging can mitigate potential inadvertent ingestion by consumers, especially children who may unintentionally swallow these products.
- The final product packaging system should contain, preserve, protect, and deliver. There are product risks from improperly stored and shipped products.
 - If not stored in the proper container or package, alcohol-based hand sanitizer products can also experience increased evaporative loss that may decrease its effectiveness^{vi}.
 - Temperature and light variations may impact alcohol-based hand sanitizer quality^{vii}. Additionally, alcohol-based hand sanitizer can become a fire safety hazard, as its base chemicals are flammable^{viii}.
 - Ingestion by children can be avoided by properly storing alcohol-based hand sanitizer.

Regulatory and Public Health Strategies to Increase Trust

- With the rapid increase in alcohol-based hand sanitizer production and supply, new and increasing quality and safety issues have been identified.
- The contamination and/or substitution of methanol for ethanol and 1-propanol for 2-propanol have both been linked to quality and safety issues associated with alcohol-based hand sanitizers.
- The Drugs & Cosmetics Act of 1940 and rules under the Central Licensing Authority, Central Licensing Approving Authority, and State Licensing Authority provide the regulatory framework in India.
 - In Gujarat, India, the Food and Drug Control Administration (FDCA) made substantial progress in response to COVID-19 through innovative regulatory approach, expediated approvals, preventive care promotion, increased surveillance, and new partnerships. Specifically, the FDCA:
 - Advanced critical tools for alcohol-based hand sanitizer enforcement: mobile drug testing lab, handheld instruments, rapid microbiological testing system, and mass SMS alerts for effective recall; and
 - Implemented enforcement activities of price monitoring and raids on illegal and spurious drugs/cosmetics.
- The U.S. FDA has identified adverse events including accidental ingestion, ocular injuries, and burns, as well as quality issues such as contamination and sub-potency, mislabeling of products, and packaging in food and drink containers.
 - U.S. FDA monograph for “topical consumer antiseptic rub products” (such as hand sanitizers) set certain requirements for safety and efficacy. Similarly, USP standards for identity, strength and purity help ensure product quality and therefore contribute to patient and consumer safety.
 - To address the dramatic increase in demand and the flood of new products due to COVID-19, the U.S. FDA [issued](#) four guidance documents and a “do-not-use” list of hand sanitizer products for consumers.

- There is a new identity testing [requirement](#) to test for methanol that is included in the USP Alcohol and Dehydrated monographs, and the FDA coordinated with USP to update these monographs.
- To comply with CGMP regulations:
 - Identity testing must be conducted to verify each component of a drug product. See 21 CFR 211.84(d)(1);
 - Each component of a drug product shall be tested for conformity with all appropriate written specifications for purity strength, and quality, unless the certificates of analysis provided by suppliers have been appropriately validated. See 21 CFR 211.84(d)(2); and
 - If Methanol detection and quantification is part of the Identification test, the CGMP regulations at 21 CFR 211.84(d)(1) would require that manufacturers of drug products detect and quantify any Methanol present for each lot of Alcohol received.
 - Furthermore, manufacturers of Alcohol could not deviate from the Methanol limit since this would be an aspect of identity. In contrast, if Methanol detection and quantification is part of an impurity test, a manufacturer need not include as part of its identity testing the detection and quantification of Methanol in the Alcohol.

Standards, Current Good Manufacturing Practices (CGMP), and Mitigation Strategies

- Compliance with USP's science-based standards, which constantly evolve through public input, help companies in this growing market segment detect adulteration.
 - Using USP standards helps to ensure that patients receive quality alcohol-based hand sanitizers and other drug products.
 - USP has revised its alcohol monographs to address methanol contamination. The USP identity test for alcohol now includes a specific identity test for methanol content.
- USP's services and programs, such as the USP Ingredient Verification Program, give industry tools that help qualify their supply chain, ensure quality, and reduce risk.
 - The USP Ingredient Verification Program can help enhance a manufacturer's competitive position and brand recognition by promoting the manufacturer's commitment to produce quality products for consumers
- Labels are essential for product identification. They must be clear, easy to read, and unable to be smudged.
 - Labels of hand sanitizer ingredients should align with current FDA requirements detailed in the *Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19) Guidance for Industry* Additionally, specific details such as concentration and grade (e.g. USP, FCC) should be clearly stated on the label and should be confirmed upon receipt
 - USP designation indicates that the product complies with a specific USP-NF monograph

If complies with USP monograph it must have 1. specific monograph name on label and 2. any additional labeling requirements described in the specific monograph.

Quality in Action

- Manufacturer Perrigo shared a case study about their rapid response to an urgent public health request. They quickly developed, produced, tested, and donated 1 million alcohol-based hand sanitizer units by June 2020.
- As a company that was not making alcohol-based hand sanitizer before the pandemic, some of their key considerations included:
 - Adding capabilities for long-term viability,

- Making their own gel-based formula as a New Product Development rather than FDA Guidance Formula, “Policy for Temporary Compounding of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency” ,
- Choosing three bottle options for packaging to have insurance in case of supply chain disruptions,
- Understanding how alcohol and handling of the product will impact the printed ink on the label, and
- Meeting the same standards as all other products.

Q&A Responses

1. Benzyl alcohol, an antimicrobial is also in the family of alcohol, can you please elaborate on whether a small amount with ethanol is acceptable?

U.S. CDC and WHO recommend the use of isopropyl alcohol or ethanol when preparing alcohol-based hand sanitizers. The USP formulas for alcohol-based hand sanitizers are based on WHO and CDC recommendations. USP does not have any information on the suitability of benzyl alcohol for hand sanitizers.

ⁱ CDSCO (11 Jan 2021). “Alerts.” <https://cdsco.gov.in/opencms/opencms/en/Notifications/Alerts/>

ⁱⁱ IDDO Medicine Quality Monitoring Globe Index (2020)

ⁱⁱⁱ CDSCO (11 Jan 2021). “Alerts.” <https://cdsco.gov.in/opencms/opencms/en/Notifications/Alerts/>

^{iv} IDDO Medicine Quality Monitoring Globe Index (2020)

^v <https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e1.htm>

^{vi} USP Chapter <659> Packaging and Storage Requirements

^{vii} USP Chapter <671> Containers—Performance Testing

^{viii} <https://www.fire.tc.faa.gov/pdf/TN10-19.pdf>