



UNDERSTANDING ACETONE SOURCES AND TOXICITY LIMITS

Solvents are used in the extraction of spices, essential oils, flavor compounds, and pharmaceutical production. The FDA requires residual solvent testing on any food or drug that has been exposed to solvents. The FDA divides the solvents into Class 1, 2, and 3. Acetone is listed as a Class 3 solvent by the FDA. Class 3 solvents present no known human health hazard at commonly accepted levels in the pharmaceutical industry.¹

Acetone is a very common solvent in manufacturing and also naturally occurring in plants and trees. It is a product in the enzymatic breakdown of fats, and small amounts naturally occur in some foods (fruits, vegetable, nuts) (<5 ppm).² Other sources of trace amounts of Acetone in manufacturing could be a result of oxidation of Isopropanol in the presence of heat and a metal catalyst. Isopropanol has also been known to oxidize in the presence of heat and sodium hypochlorite (bleach), an oxidizing agent.³

Stainless steel is commonly used in manufacturing due to its resistance to oxidation. It is made of up of mainly iron, consisting of roughly 10% chromium. The chromium reacts with an oxygen source (air, water, etc.) to produce a protective layer over the surface. That thin layer of chromium oxide on the surface can be maintained, but under the right circumstances can be susceptible to corrosion, making it reactive. Mechanical damage or chemical attack can lead to localized corrosion. Some acids, notably hydrochloric and sulfuric acid, can attack the surface and cause corrosion.

Prolonged contact with chlorine ion (salts, bleach) can also cause corrosion of the chromium layer. The fact this chromium layer requires contact with oxygen (in the air) to create the protective chromium oxide layer, damage to the steel may hinder contact with oxygen, therefore making those areas more susceptible to corrosion.⁴ It is possible those areas can provide a source of oxidation to Isopropanol in the right environment.

Acetone is a liquid at room temperature but is very volatile, and at room temperature can evaporate. Environmental contamination (adjacent areas using Acetone, trace amounts in car exhaust and fuel) can also be a source of Acetone in manufacturing. Acetone has also been noted to be a trace breakdown product of pinene, a common terpene.⁵ USP <467>, which applies to finished drug products, regard class 3 solvents as low risk to human health. The presence of 5000 ppm or less is considered acceptable exposure by the FDA.¹ However, 21CFR173.210, which applies to food additives and coloring, requires Acetone to be present at less than 30 ppm.

Currently the cannabis industry has no federal guidance to follow due to the legal standing of cannabis on a federal level. States are left to develop their own regulations and limits on residual solvents presence. Colorado has set limits for certain solvents, i.e. n-butane - <50ppm.⁷ But Acetone has not been assigned limits. Washington requires <500 ppm for all solvents in a finished cannabis extract.⁸ Limits can vary widely from state to state. It is important to know your process as a manufacturer and understand all steps in the manufacturing process to ensure a safe product. Acetone, like many chemicals, is naturally present in many foods and plants, as well as in environment. It is also important to understand at what level solvents are a concern and in what way they are going to be utilized.

REFERENCES

¹ Guidance for Industry, Residual Solvents in Drug Products Marketed in the United States, Food and Drug Administration (Nov 2009); USP (United States Pharmacopeia) Chapter <467> Residual Solvents.

² Public Health Statement: Acetone, www.atsdr.cdc.gov; toxtown.nlm.nih.gov (Center for Disease Control and National Institute of Health information links)

³ E.C. Wagner, Philadelphia College of Pharmacy and Science, *Journal of Chemical Education*

⁴ Passivity and Its Breakdown on Stainless Steels and Alloys, *Surface and Interface Analysis*, Volume 33 (October 2002)

⁵ Measurement of Acetone and Other Gas Phase Product Yields from OH-initiated Oxidation of Terpenes by PTR-MS, *Atmospheric Environment*, Volume 35 (December 2001)

⁶ Code of Federal Regulations (CFR), Title 21-Food and Drugs, Part 173.210 Secondary Direct Food Additives Permitted in Food for Human Consumption

⁷ State of Colorado, MED Rule R712 (E)(2), R605, and R1501 (C)(4)

⁸ Washington State Liquor Control Board, WAC Chapter 314-55-104