UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: December 31, 2021

SUBJECT: IN-11369; Potassium Acetate: Human Health Risk and Ecological Effects Assessment of Food Use Pesticide Inert Ingredient

CAS Reg. No. 127-08-2
PC Code: 900897
Decision 556596

FROM: Deirdre Sunderland, MHS, Industrial Hygienist
Chemistry, Inerts & Toxicology Assessment Branch (CITAB)
Registration Division (RD)

THROUGH: Evisabel Craig, PhD, DABT, Inert Ingredients Team Leader
CITAB/RD

Digitally signed by EVISABEL CRAIG
Date: 2022.02.03 15:04:22 -05'00'

TO: Kerry B. Leifer, Chief
CITAB/RD

Table of Contents

1. Executive Summary 3
2. Background 4
3. Ingredient Profile 4
   3.1 Phyiscal and Chemical Properties 4
   3.2 Analog Chemicals 5
   3.3 Metabolism and Pharmacokinetics 5
4. Hazard Characterization 6
   4.1 Acute Toxiciy 7
   4.2 Subchronic Toxicity 7
   4.3 Chronic Toxicity 8
   4.4 Reproductive and Developmental Toxicity 8
   4.5 Neurotoxicity 8
   4.6 Mutagenicity/Cytotoxicity 9
   4.7 Carcinogenic Potential 9
   4.8 Endpoint Selection and Levels of Concern 10
   4.9 FQPA Safety Factor 10
5. Exposure 10
   5.1 Dietary 10
   5.2 Cancer 11
   5.3 Residential 11
   5.4 Occupational 11
6. Aggregate Risk 11
7. Cummulative Exposure 11
8. Environmental Fate 11
9. Ecological Effects 12
10. Risk Characterization 13

Bibliography 14
APPENDIX A. EPISuite v 4.10 16
APPENDIX B. OECD QSAR Toolbox 19

1. EXECUTIVE SUMMARY

In October 2019, SciReg, Inc., on behalf of Valagro S.p.A., submitted a petition to the Environmental Protection Agency, herein referred to as the Agency or EPA, to amend 40 CFR 180.920, by establishing an exemption from the requirement of a tolerance for the use of the inert ingredient potassium acetate (CAS Reg. No. 127-08-2) in pesticide formulations applied pre-harvest.

Potassium acetate is the potassium salt of acetic acid. It has numerous uses including use in cleaning products, pharmaceuticals, various industrial/manufacturing processes, use as a de-icer, and as a food additive. The purpose of potassium acetate as an inert ingredient in pesticide formulations is as a plant nutrient.

Acetic acid and acetates are naturally present in various foods and in the body; however, limited data exist for potassium acetate. As one of the salts of acetic acid, sodium acetate, like potassium acetate, dissociates in aqueous solutions to the acetate ion and a counter ion, in this case sodium. Based on their similarities (e.g., physical/chemical properties, chemical structure, subsequent dissociation into the acetate ion and corresponding anion) data on sodium acetate has been used in this risk assessment to support the safety determination for potassium acetate when chemical specific data was not available.

Potassium acetate has low acute oral, dermal, and inhalation toxicity. Skin irritation studies showed no effect of treatment. Skin sensitization studies were not provided. Eye irritation studies on potassium acetate resulted in mild eye irritation.

The Joint FAO/WHO Expert Committee on Food Additives (JEFCA) evaluated acetic acid and its potassium and sodium salts as food additives (acidity regulator and preservative) and determined an Acceptable Daily Intake (ADI) of "not limited" for acetic acid and its potassium and sodium salts. Repeat dose oral toxicity studies on potassium acetate were not found in the database. A 4-week oral study with sodium acetate in rats showed no adverse effects up to the highest dose tested, 3600 mg/kg/day.

While no developmental or reproductive studies were conducted with potassium acetate, sodium acetate was tested via oral gavage at a dose level of 1,000 mg/kg/day on pregnant mice. No significant maternal or fetal effects were seen. There was no evidence of carcinogenicity or mutagenicity in any of the studies presented. In addition, no neuropathological changes or effects were reported in any of the studies. Therefore, there is low concern for carcinogenicity or neurotoxicity with potassium acetate.

No endpoint of concern was determined in any of the studies up to the limit dose of 1000 mg/kg/day. Since no endpoint of concern was identified in acute or repeated-dose toxicity studies at the limit dose or higher and because acetic acid and acetates are ubiquitous in the environment, a quantitative risk assessment for potassium acetate was not performed. As part of its qualitative assessment, the Agency did not use safety factors for assessing risk, and no additional safety factor is needed for assessing risk to infants and children.

While residential and occupational exposures are possible, there are no toxicological effects of concern in available studies at the limit dose and therefore, it is not necessary to conduct a quantitative assessment of residential (non-occupational) exposures and risks. Similarly, a quantitative occupational risk assessment is not necessary.

The Agency also concluded that potassium acetate does not pose an ecological risk to terrestrial or aquatic species. After evaluating the toxicity studies, along with the expected exposure from the use of this chemical as inert ingredient in pesticide products, EPA concludes that there is a reasonable certainty that no harm will result to the general population, including infants and children, from aggregate exposure to residues of potassium acetate when used as an inert ingredient in pesticide formulations under 40 CFR 180.920.

2. BACKGROUND

In October 2019, SciReg, Inc., on behalf of Valagro S.p.A., submitted a petition to the EPA to amend 40 CFR 180.920, by establishing an exemption from the requirement of a tolerance for the use of the inert ingredient potassium acetate (CAS Reg. No. 127-08-2) in pesticide formulations applied pre-harvest. Potassium acetate is the potassium salt of acetic acid. The salts of acetic acid are formed by the acetate ion and different anions, such as potassium and sodium. The proposed use of potassium acetate as an inert ingredient in pesticide products is as a plant nutrient.

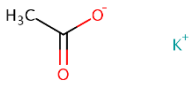
Potassium acetate has various uses including use in cleaning products, pharmaceuticals, various industrial/manufacturing processes, use as a de-icer, a fragrance ingredient, and use as a food additive. It is approved by the US Food and Drug Administration (FDA) under 21 CFR 172.515 for use as a "synthetic flavoring substances and adjuvants". In 1973 and maintained in 1997, the Joint FAO/WHO Expert Committee on Food Additives (JEFCA) evaluated acetic acid and its potassium and sodium salts as food additives (acidity regulator and preservative) and determined an Acceptable Daily Intake (ADI) of "not limited" for acetic acid and its potassium and sodium salts.

Acetic acid or acetates are present in most plants and animal tissue. (SCOGS, 1977) Acetic acid makes up the characteristic acid of vinegar. According to the FDA's Compliance Policy Guide (CPG) Sec 525.825, *Vinegar, Definitions*, the FDA requires vinegar to contain at least 4% acetic acid (i.e., at least 4g acetic acid/100ml). Commonly used vinegars may range up to 8% acetic acid. (Harvard, 2021)

3. INERT INGREDIENT PROFILE

3.1. Physical and Chemical Properties

Some of the physical and chemical characteristics of potassium acetate along with the chemical structure and nomenclature, are found in Table 1 below. In aqueous solution, potassium acetate dissociates to potassium and acetate ions. The acetate ion is the conjugated base (i.e., the species formed after an acid donates a proton) of acetic acid.

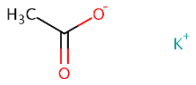
Table 1. Physical and Chemical Properties of Potassium Acetate		
Parameter	**Value**	**Reference**
Synonyms	Acetic acid, potassium salt; Potassium ethanoate	CIR
Structure		EPA
CAS Reg. No.	127-08-2	EPA
Molecular Formula	$C_2H_3KO_2$	EPA
Molecular Weight	98.14 g/mol	CIR
Physical State	Solid, Crystalline or powder	ECHA
Melting Point	292°C	ECHA, CIR
Density	1.6 g/cm^3 @ 20°C	ILO
Vapor Pressure	1.37 x 10-8 mmHg @20°C 1.37 x 10-8 mmHg @25°C	CIR, estimated ECHA, site EPI Suite
Water Solubility	265 g/100ml solid @20°C 2530 g/L @20°C	ILO ECHA
Log K_{ow}	-3.72	EPI Suite v 4.10

ILO: https://www.ilo.org/dyn/icsc/showcard.display?p_lang=en&p_card_id=0547&p_version=2
EPA: https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID7027043#details

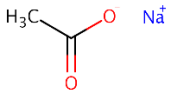
3.2. Analog Chemicals

As one of the salts of acetic acid, sodium acetate, like potassium acetate, dissociates in aqueous solution to the acetate ion and a counter ion, in this case sodium. Toxicity data on potassium acetate is limited and therefore, based on their similarities (e.g., physical/chemical properties, chemical structure, subsequent dissociation into the acetate ion and corresponding anion) much of this risk assessment relies on data for sodium acetate when data on potassium acetate was not available.

Potassium Acetate



Sodium Acetate



According to EPA's CompTox Chemicals Dashboard website, potassium acetate, has a similarity threshold of at least 0.8 (criteria used) with sodium acetate.

3.3. Metabolism and Pharmacokinetics

Studies on the absorption, distribution, metabolism, and excretion (ADME) of potasssium acetate are not available. Instead, a study on sodium acetate was used to predict how potassium acetate would behave in the body. Both potassium acetate and sodium acetate are hydrolyzed to acetate and the corresponding ion in aqueous solutions therefore, a study on sodium acetate is considered relevant.

In this study, presented in the ECHA dossier for sodium acetate, sodium acetate was administered by gavage to male and female Wistar rats. Rats were placed in metabolism cages and carbon dioxide was trapped by sodium hydroxide solution and then analyzed for radioactivity. Urine and feces were also collected and analyzed for radioactivity. Most of the radioactivity was recovered in the form of carbon dioxide (79 to 95%). "Only a small amount of the radioactivity in the body was found in urine and faeces." The amount recovered from males in the first 24 hours was "considerably less" than that found for females, indicating that, "Male rats apparently tend to fix more of the radioactivity in the body tissues and, the acetate carbons were not turned over as rapidly as in the females."

There were two separate rates for the elimination of radiolabeled carbon dioxide. The initial rate of elimination (1- 8 hours post-administration) was rapid followed by a much slower rate of elimination. The half-lives for these two rates were 4 to 6 hours and 25 hours, respectively. According to the ECHA summary, the two separate rates of elimination represent two routes of metabolism: "the initial rate of elimination is probably due to the direct reaction of acetate with CoA-SH to form acetyl-CoA which subsequently is oxidized" to carbon dioxide (CO_2) through the tricarboxylic acid cycle. The report goes on to state that the slower rate of elimination is "probably derived from acetate carbons which are incorporated into other metabolites, such as fatty acids and amino acids which are subsequently catabolized to CO_2."

The counter ion, potassium, is the most abundant intracellular cation in the body and is present in all body tissues. (NIH, 2021) It is an essential nutrient necessary for normal cellular activity "because of its role in maintaining intracellular fluid volume and transmembrane electrochemical gradients". (NIH, 2021) It plays a vital role in the functioning of the kidneys and heart, it is necessary for contraction of the muscles, and the transmission of messages through the nervous system.

In one study, approximately 90% of the potassium ion was absorbed when 90 mEq/day was ingested. (Agarwal et al., 1994) The majority of intestinal absorption occurs in the small intestine with minimal absorption in the colon. The major route of excretion of the potassium ion is through the kidneys. The kidney is primarily responsible for maintaining potassium levels in the body by matching potassium intake with potassium excretion. Potassium is freely filtered by the glomerulus and is actively reabsorbed in the proximal tubules but regulation occurs mostly at the collecting ducts. Both aldosterone and antidiuretic hormone (ADH) increase potassium loss into the urine. Fecal potassium ion excretion, along with loses through sweat, average about 10% of intake. (Agarwal, et al. 1994 and Palmer et al., 2015).

4. HAZARD CHARACTERIZATION

Limited studies are available for potassium acetate. In liquid, potassium acetate dissociates to potassium and the acetate ions. Acetate ions will react with water and form acetic acid. These are naturally occuring and necessary for human life. This hazard assessment uses studies on potassium acetate, when available, but also relies on data for sodium acetate (CAS Reg. No. 127-09-3) through a read across approach discussed in Section 3.2.

4.1. Acute Toxicity

4.1.1. Acute Oral Toxicity

A singe oral gastric intubation of potassium acetate was administered to five nonfasted, Carworth-Wistar male rats. The animals were observed for signs of toxicity and mortality for 14 days. The Lethal Dose for 50% of the animals (LD_{50}) for potassium acetate was determined to be 3,250 mg/kg. (Smyth et al., 1962 and Smyth et al., 1969)

4.1.2. Acute Dermal Toxicity

No acute dermal toxicity studies were submitted for potassium acetate. However, according to the Cosmetic Ingredient Review (2012) document on the safety review for a number of chemicals including various alkyl acetates, acetic acid, and acetate salts such as potassium acetate; the acute subcutaneous LD_{50} for administration of sodium acetate to mice was 3,200 mg/kg.

4.1.3. Acute Inhalation Toxicity

According to the Cosmetic Ingredient Review (2012) the acute inhalation LC_{50} for sodium acetate in rats was reported to be greater than 30 g/m^3. No other details were provided.

4.1.4. Skin Irritation

A dermal irritation test using the Organisation for Economic Cooperation and Development (OECD) Test Guideline 404 was conducted with three New Zealand White rabbits using a 50% water solution of potassium acetate. (ECHA) A 25 cm^2 exposure area was created and 0.5ml of the test substance was applied, covered with a semi-occlusive dressing, and after 4 hours, the area was washed with water. No signs of skin irritation were observed throughout the 72-hour study period.

4.1.5. Eye Irritation

An eye irritation test (OECD 405) was conducted with three New Zealand White rabbits using a 50% water solution of potassium acetate. (ECHA) Animals were treated with 0.1ml of the of the test solution which remained in the eye for 24 hours. After 24-hours the eyes were washed with a NaCl solution. Observations were made at 1, 24, 48, and 72 hours post exposure. Only the observations at 72 hours were reported in the ECHA summary. At 72-hours there was no effect on the cornea or iris. The conjunctivae showed “some blood vessels show a marked hyperemia” resulting in a score of 1 for the conjunctivae.

4.1.6. Skin Sensitization

No skin sensitization data was found in the database for potassium acetate.

4.2. Subchronic Toxicity

The ECHA dossier for potassium acetate outlined some studies conducted with sodium acetate that have been omitted from this review because the values tested were extremely low and did not lead to a determination of toxicity. Only those studies which are relevant for decision making and support the safety findings have been included here.

The full study report was not available; however, according to the ECHA summary provided, sodium acetate was tested over a 4-week period in male rats exposed to 3600 mg/kg/day via the diet. No effects were documented in the summary and the No Observed Adverse Effect Level (NOAEL) listed in the report was 3,600 mg/kg/day (highest and only dose tested). The ECHA report converts this value into an equivalent value for potassium acetate and gives a NOAEL of 4307 mg/kg/day for potassium acetate.

4.3. Chronic Toxicity

No chronic studies are available for potassium or sodium acetate; however, there were no structural alerts for carcinogenicity for potassium acetate when evaluated using the OECD QSAR Toolbox, version 4.5 (Appendix B). The model uses Quantitative Structure-Activity Relationships (QSAR) for estimating the properties of a chemical from its molecular structure.

4.4. Reproductive and Developmental Toxicity

In 1987 an article was published in *Teratogenesis, Carcinogenesis, and Mutagenesis* by members of the EPA's Health Effects Research Laboratory. (Kavlock, et al., 1987) The article described an *in vivo* screening procedure used to evaluate 46 chemicals for teratology. This screening method, developed to address the requirement of the Toxic Substances Control Act (TSCA), was then compared to known developmental toxicity for the chemicals.

In this study, sodium acetate was administered to thirty pregnant female CD-1 mice via oral gavage at a dose level of 1,000 mg/kg/day for five days from gestation days 8 to 12. Another group of 40 mice served as the control. On postnatal days 1 (day 20 of gestation) and 3, the litters were counted and weighed. There were no significant effects in the criteria evaluated (e.g., percent pregnant, percent died, and percent resorbed). There were also no significant differences in the neonatal effects evaluated (i.e., number live pups and pup weights on postnatal days 1 and 3). Therefore, sodium acetate was considered non-teratogenic in this study. No maternal toxicity was seen.

The article indicated that the results of the screening test were consistent with "standard test results using the mouse". The article did not outline those "standard tests" except to say that it was largely based on literature reviews and only published mouse data was used.

4.5. Neurotoxicity

Although no specific neurotoxicity studies were found in the database for potassium acetate, no signs of neurotoxicity were observed in any of the studies reviewed. Therefore, there is low concern for neurotoxicity for potassium acetate.

4.6. Mutagenicity/Cytotoxicity

4.6.1. Select Committee on GRAS Substances (SCOGS) Report

According to SCOGS report, "Sodium acetate was tested for mutagenic activity in a series of *in vitro* microbial assays using strains TA 1535, 1537, and 1538 of *Salmonella typhimurium* and strain D4 of *Saccharomyces cerevisiae* with and without metabolic activation by mouse, rat, or monkey liver homogenates. This substance did not exhibit mutagenic activity in any of the assays employed in this evaluation." (SCOGS, 1977) Similarly, the studies outlined below showed no evidence of mutagenicity.

4.6.2. Chromosome Aberration Test

An *in vitro* chromosomal aberration test was conducted with sodium acetate using a Chinese hamster fibroblast cell line. (Ishidate, et al., 1984) The cells were exposed to the sample at three different dose levels for 24 and 48 hours. The maximum dose was selected by a preliminary test in which the dose needed for 50% cell-growth inhibition was estimated using a cell densitometer. No metabolic activation was used. This study was negative for chromosomal aberrations.

The incidence of polyploid cells, as well as of cells with structural chromosomal aberrations, such as chromatid or chromosome gaps, breaks, exchanges, ring formations, fragmentations, and others was recorded on each culture plate. Untreated cells and solvent-treated cells served as negative controls. "The results were considered to be negative if the incidence was less than 4.9%, equivocal if it was between 5.0 and 9.9%, and positive if it was more than 10.0%." The incidence of polyploid cells for sodium acetate was 1.0% and the percent of cells with structural chromosomal aberrations were 0.0%; indicating a negative result.

4.6.3. Bacterial Reverse Mutation Assay

A reverse mutation assay was conducted with sodium acetate using S. *typhimurium* strains TA92, TA1535, TA100, TA1537, TA94, and TA98 according to the Ames, McCann, and Yamasaki (1975) method. (Ishidate, et al., 1984) The liver microsome fraction (S-9) was prepared using the liver of Fischer rats. "Cells cultured overnight were pre-incubated with both the test sample and the S-9 mix for 20 minutes at 37°C before plating." After two days of incubation at 37°C, the number of revertant (his+) colonies was evaluated. "The result was considered positive if the number of colonies found was twice the number in the control (exposed to the appropriate solvent or untreated)." Sodium acetate was not mutagenic in this study.

4.7. Carcinogenic Potential

There was no evidence of carcinogenicity in the studies reviewed and all genotoxicity studies on sodium acetate were negative. In addition, there were no structural alerts for toxicity for potassium acetate when evaluated using the OECD QSAR Toolbox (Appendix B). Therefore, there is low concern for carcinogenicity for potassium acetate.

4.8. Endpoint Selection and Levels of Concern

In 1973 (and maintained in 1997), the Joint FAO/WHO Expert Committee on Food Additives (JEFCA) evaluated acetic acid and its potassium and sodium salts as food additives (acidity regulator and preservative) and determined an Acceptable Daily Intake (ADI) of "not limited" for acetic acid and its potassium and sodium salts. Similarly, no adverse effects were seen in any of the available studies at or below the limit dose of 1000 mg/kg/day; therefore, no endpoint of concern has been identified for acute, subchronic, or chronic toxicity. Since no endpoint of concern was identified a quantitative risk assessment for potassium acetate is not necessary.

4.9. FQPA Safety Factor Considerations

FFDCA Section 408(b)(2)(c) provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA safety factor (SF). In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

The available acute and repeat dose toxicity studies on potassium acetate indicate that it has low toxicity with no adverse effects of treatment seen at the limit dose of 1000 mg/kg/day. There is no indication, based upon the available data, that potassium acetate is neurotoxic or immunotoxic and therefore, would not result in increased susceptibility in infants or children. As part of its qualitative assessment, the Agency did not use safety factors for assessing risk, and no additional safety factor is needed for assessing risk to infants and children. Taking into consideration all available information, there is no concern, at this time, for increased sensitivity to infants and children to potassium acetate when used as inert ingredient in pesticides formulations.

5. EXPOSURE

Humans are exposed to acetic acid and potassium because they are ubiquitous in the environment and are present in a variety of foods. Potassium acetate is intended as a plant nutrient and will be applied preharvest. The overall exposure from preharvest use of potassium acetate as an inert ingredient is not expected to significantly increase the overall exposure to humans as it is expected to be utilized by the plant as a nutrient source. In addition, no endpoint of concern was identified at the limit dose of 1000 mg/kg/day or higher; therefore, a quantitative risk assessment was not necessary.

5.1. Dietary Exposure

Although dietary exposure to potassium acetate may occur from eating foods treated with pesticide formulations containing this inert ingredient and drinking water containing runoff from soils containing the treated crops, no endpoint of concern was identified and therefore, a quantitative dietary exposure assessment for potassium acetate was not conducted.

5.2. Cancer Exposure

Based on the available toxicity data presented in Section 4.7, potassium acetate is not expected to be carcinogenic. Therefore, a cancer dietary exposure assessment is not necessary to assess cancer risk.

5.3. Residential (Non-Occupational) Exposure

The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). The proposed use of potassium acetate will be limited to pesticide applicators. Potential residential uses in the future would also be protected because there are no toxicological effects of concern in available studies and therefore, it is not necessary to conduct a quantitative assessment of residential (non-occupational) exposures and risks.

5.4. Occupational Exposure

According to Valagro S.p.A., non-dietary exposure to potassium acetate as proposed will be limited to pesticide applicators. Applicators will have little to no exposure to potassium acetate as they will be required to wear appropriate personal protection equipment prescribed by the product label. In addition, the Agency has reviewed the available toxicological information for potassium acetate and identified no toxicological endpoints of concern, therefore a quantitative occupational risk assessment is not necessary.

6. AGGREGATE RISK

Because no adverse effects, attributable to a single or repeat exposure, were seen at the limit dose in the toxicity database for the potassium acetate, a qualitative risk assessment was conducted and subsequently, it is not necessary to aggregate dermal and inhalation residential exposures with estimated dietary exposures.

7. CUMMULATIVE EXPOSURE

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide's residues and “other substances that have a common mechanism of toxicity.” EPA has not found potassium acetate to share a common mechanism of toxicity with any other substances, and potassium acetate does do not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that the potassium acetate does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at http://www.epa.gov/pesticides/cumulative.

8. ENVIRONMENTAL FATE

Acetic acid/acetates are present in most plant and animal tissues in small but detectable amounts. (SCOGC, 1977 and Burdock, 2010) The predicted environmental values found in Table 2 were taken from EPA's EPISuite v.4.10, and PubChem.

Table 2: Environmental Fate Characteristics of Potassium Acetate		
Parameter	**Value**	**Source**
Vapor Pressure (VP)	1.37 x 10^{-8} mmHg @ 25°C	USEPA EPISuite v.4.10
Henry's Law Constant	1.793 × 10^{-10} Pa m^3/mol	USEPA EPISuite v.4.10
Water Solubility	256 g/100ml @ 20°C 100 g/100ml @ 25°C	Pubchem* USEPA EPISuite v.4.10
Log Koc **Kow method**	-1.902	USEPA EPISuite v.4.10
Log Kow	-3.72	USEPA EPISuite v.4.10
Ready Biodegradability	Yes	USEPA EPISuite v.4.10
BCF (L/kg wet-wt)	3.162	USEPA EPISuite v.4.10
Fugacity Model Compartment/Mass Amount (%) **Air** **Water** **Soil** **Sediment**	Mass Amt (%) 3.05 x 10^{-7} 33.5 66.5 0.059	USEPA EPISuite v.4.10

*Pubchem: https://pubchem.ncbi.nlm.nih.gov/compound/Potassium-acetate

According to the EPA Dashboard, potassium acetate has a predicted biodegradation half-life of approximately 4.6 days. The predicted bioconcentration factor (BCF) is listed as 2.47 with a predicted soil adsorption coefficient (Koc) of 1.01. The BCF, as calculated according to EPI Suite (i.e., BCFWIN v3.00) is 3.162.

Biodegradability on sodium acetate was accessed using a non-adapted activated sludge for the test item over a test period of 28 days in a DOC-Die-Away test. At 7 days biodegradation reached 86% and at 28 days, biodegradation reached 99%. (ECHA) Potassium acetate is expected to readily biodegrade.

9. ECOLOGICAL EFFECTS

Ecological toxicity studies described below have been outlined in the ECHA dossier for potassium acetate. Only a brief summary is provided here.

9.1. Fish Toxicity

The 96h-LC_{50} (Lethal Concentration) for potassium acetate in an OECD 203, acute toxicity study, with *Brachydanio rerio* (i.e., *Danio rerio* or Zebra fish) was greater than 496.35 mg/L. Therefore, potassium acetate is not expected to be toxic to fish.

9.2. Invertebrate Toxicity

The 48h-EC_{50} (Effect Concentration) was greater than 459.5 mg/L for potassium acetate in an OECD 202 (Acute Immobilization Test) with *Daphnia magna.* Potassium acetate is not expected to be toxic to aquatic invertebrates.

9.3. Algal Toxicity

The 72-hour EC_{50} value for potassium acetate was greater than 500 mg/L when tested with *Skeletonema costatum*. The NOEC value was estimated to be 500 mg/L.

10. RISK CHARACTERIZATION

While dietary (food and drinking water), residential, and occupational exposure are possible, there are no toxicological effects of concern in available studies and therefore, it is not necessary to conduct a quantitative assessment of dietary, residential (non-occupational), or occupational exposures and risks. As part of its qualitative assessment, the Agency did not use safety factors for assessing risk, and no additional safety factor is needed for assessing risk to infants and children.

The Agency also concluded that potassium acetate does not pose an ecological risk to terrestrial or aquatic species. Potassium acetate is readily biodegradable, has low toxicity to aquatic organisms, and is not expected to be persistent, bioaccumulable, or be toxic (PBT).

After evaluating the toxicity studies along with the expected exposure from the use of this chemical as inert ingredient in pesticide products, EPA concludes that there is a reasonable certainty that no harm will result to the general population, including infants and children, from aggregate exposure to residues of potassium acetate when used as an inert ingredient in pesticide formulations under 40 CFR 180.920.

Bibliography

Agarwal R., Afzalpurkar R., and Fordtran J.S. Pathophysiology of potassium absorption and secretion by the human intestine. Gastroenterology. 1994 Aug;107(2):548-71. doi: 10.1016/0016-5085(94)90184-8. PMID: 8039632. Retrieved from https://pubmed.ncbi.nlm.nih.gov/8039632/

Burdock, G. A. (2010) Fenaroli's Handbook of Flavor Ingredients. 6th Ed. CRC Press.

Cosmetic Ingredient Review (CIR) (2012) Heldreth, B., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D., Marks Jr, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., and Andersen, F. A. (2012) Final Report of the Cosmetic Ingredient Review Expert Panel on the Safety Assessment of Methyl Acetate. *International Journal of Toxicology*. 31(Supplement 1) 112S-1136S.

European Chemicals Agency (ECHA) Dossier for Potassium Acetate retrieved from https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15104, on 12/30/2021

European Chemicals Agency (ECHA) Dossier for Sodium Acetate retrieved from https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15311/7/2/2, on 11/10/2021

Harvard School of Public Health (2021) The Nutrition Source: Featured Foods- Vinegar, retrieved on 12/28/21 from https://www.hsph.harvard.edu/nutritionsource/food-features/vinegar/

Ishidate, M., Sofuni, T. JR., Yoshikawa, K., Hayashi, M., Nohmi, T., Sawada, M., and Matsuoka, A. (1984) Primary Mutagenicity Screening of Food Additives Currently used in Japan. *Food and Chemical Toxicology.* Vol. 22, No. 8, pp. 623-636.

Kavlock, R.J., Short, R.D., and Chernoff, N. (1987) Further Evaluation of an *In Vivo* Teratology Screen. *Teratogenesis, Carcinogenesis, and Mutagenesis*. Volume 7. Pages 7-16.

Palmer, Biff F. (2015) Regulation of Potassium Homeostasis. Clinical Journal of American Society of Nephrology. June 5, 2015; 10(6): 1050-1060. Published online 2014 Apr 10. doi: 10.2215/CJN.08580813 retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4455213/#:~:text=Potassium%20is%20freely%20filtered%20by,and%20water%20(Figure%203).

The Select Committee on GRAS Substances (SCOGS) (1977) Evaluation of the Health Aspects of Acetic Acid, Sodium Acetate, and Sodium Diacetate as Food Ingredients. Prepared for the Bureau of Foods, Food and Drug Administration, Department of Health, Education, and Welfare Washington, D. C. Contract No. FDA 223-75-2004 by Life Sciences Research Office, Federation of American Societies for Experimental Biology. Bethesda, Maryland 20014

Smyth Jr., H. F., Carpenter, C.P., Well, C.S., Pozzani, U.C., and Striegel, J.A. (1962) Range-Finding Toxicity Data: List VI, American Industrial Hygiene Association Journal, 23:2, 95-107, DOI: 10.1080/00028896209343211

Smyth Jr., H. F., Carpenter, C.P., Well, C.S., Pozzani, U.C., Striegel J.A., and Nycum, J.S. (1969) Range-Finding Toxicity Data: List VII, American Industrial Hygiene Association Journal, Sept-Oct, 470-476

Sekizawa, J., Yasuhara, K., Suyama, Y., Yamanaka, S., Tobe, M., and Nishimura, M. (1994) A Simple Method for Screening Assessment of Skin and Eye Irritation. *The Journal of Toxicological Sciences.* Volume 19. Pages 25-35.

US Department of Health and Human Services, National Institutes of Health (NIH), Office of Dietary Supplements (2021) Fact Sheet for Health Professionals: Potassium accessed on 10/30/21 from https://ods.od.nih.gov/factsheets/Potassium-HealthProfessional/

Appendix A

EPI Suite Results For Potassium Acetate

```
CAS Number: 127-08-2
SMILES : CC(=O)(O(K))
CHEM : potassium acetate
MOL FOR: C2 H3 O2 K1
MOL WT : 98.14
------------------------------ EPI SUMMARY (v4.10) --------------------------
Physical Property Inputs:
      Log Kow (octanol-water): ------
      Boiling Point (deg C) : ------
      Melting Point (deg C) : ------
      Vapor Pressure (mm Hg) : ------
      Water Solubility (mg/L): ------
      Henry LC (atm-m3/mole) : ------

Log Octanol-Water Partition Coef (SRC):
      Log Kow (KOWWIN v1.68 estimate) = -3.72

Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPVP v1.43):
      Boiling Pt (deg C): 392.35 (Adapted Stein & Brown method)
      Melting Pt (deg C): 148.53 (Mean or Weighted MP)
      VP(mm Hg,25 deg C): 1.37E-008 (Modified Grain method)
      VP (Pa, 25 deg C) : 1.83E-006 (Modified Grain method)
      MP (exp database): 292 deg C
      Subcooled liquid VP: 1.27E-005 mm Hg (25 deg C, Mod-Grain method)
                         : 0.0017 Pa (25 deg C, Mod-Grain method)

Water Solubility Estimate from Log Kow (WSKOW v1.42):
      Water Solubility at 25 deg C (mg/L): 1e+006
            log Kow used: -3.72 (estimated)
            no-melting pt equation used

Water Sol Estimate from Fragments:
      Wat Sol (v1.01 est) = 3.1301e+005 mg/L

ECOSAR Class Program (ECOSAR v1.00):
      Class(es) found:
            Neutral Organics

Henrys Law Constant (25 deg C) [HENRYWIN v3.20]:
      Bond Method : Incomplete
      Group Method: Incomplete
For Henry LC Comparison Purposes:
      User-Entered Henry LC: not entered
      Henrys LC [via VP/WSol estimate using User-Entered or Estimated
      values]:
            HLC: 1.769E-015 atm-m3/mole (1.793E-010 Pa-m3/mole)
            VP: 1.37E-008 mm Hg (source: MPBPVP)
            WS: 1E+006 mg/L (source: WSKOWWIN)

Log Octanol-Air Partition Coefficient (25 deg C) [KOAWIN v1.10]:
```

```
Can Not Estimate (can not calculate HenryLC)

Probability of Rapid Biodegradation (BIOWIN v4.10):
      Biowin1 (Linear Model) : 0.7916
      Biowin2 (Non-Linear Model) : 0.9426
Expert Survey Biodegradation Results:
      Biowin3 (Ultimate Survey Model): 3.4311 (days-weeks )
      Biowin4 (Primary Survey Model) : 4.1467 (days )
MITI Biodegradation Probability:
      Biowin5 (MITI Linear Model) : 0.7151
      Biowin6 (MITI Non-Linear Model): 0.8750
Anaerobic Biodegradation Probability:
      Biowin7 (Anaerobic Linear Model): 0.9433
Ready Biodegradability Prediction: YES

Hydrocarbon Biodegradation (BioHCwin v1.01):
Structure incompatible with current estimation method!

Sorption to aerosols (25 Dec C)[AEROWIN v1.00]:
 Vapor pressure (liquid/subcooled): 0.00169 Pa (1.27E-005 mm Hg)
 Log Koa (): not available
  Kp (particle/gas partition coef. (m3/ug)):
      Mackay model : 0.00177
      Octanol/air (Koa) model: not available
  Fraction sorbed to airborne particulates (phi):
      Junge-Pankow model : 0.0601
      Mackay model : 0.124
      Octanol/air (Koa) model: not available

Atmospheric Oxidation (25 deg C) [AopWin v1.92]:
  Hydroxyl Radicals Reaction:
      OVERALL OH Rate Constant = 0.0422 E-12 cm3/molecule-sec
      Half-Life = 253.700 Days (12-hr day; 1.5E6 OH/cm3)
Ozone Reaction:
      No Ozone Reaction Estimation
Fraction sorbed to airborne particulates (phi):
      0.0921 (Junge-Pankow, Mackay avg)
      not available (Koa method)
      Note: the sorbed fraction may be resistant to atmospheric oxidation

Soil Adsorption Coefficient (KOCWIN v2.00):
      Koc : 1 L/kg (MCI method)
      Log Koc: 0.000 (MCI method)
      Koc : 0.01253 L/kg (Kow method)
      Log Koc: -1.902 (Kow method)
       Experimental Log Koc: 0 (database)

Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v2.00]:
    Rate constants can NOT be estimated for this structure!

Bioaccumulation Estimates (BCFBAF v3.01):
  Log BCF from regression-based method = 0.500 (BCF = 3.162 L/kg wet-wt)
  Log Biotransformation Half-life (HL) = -1.5959 days (HL = 0.02536 days)
  Log BCF Arnot-Gobas method (upper trophic) = -0.032 (BCF = 0.9293)
  Log BAF Arnot-Gobas method (upper trophic) = -0.032 (BAF = 0.9293)
      log Kow used: -0.17 (expkow database)
```

Volatilization from Water:
   Henry LC: 1.77E-015 atm-m3/mole (calculated from VP/WS)
   Half-Life from Model River: 3.279E+011 hours (1.366E+010 days)
   Half-Life from Model Lake : 3.577E+012 hours (1.49E+011 days)

Removal In Wastewater Treatment:
      Total removal: 1.85 percent
      Total biodegradation: 0.09 percent
      Total sludge adsorption: 1.75 percent
      Total to Air: 0.00 percent
         (using 10000 hr Bio P,A,S)

Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	3.05e-007	6.09e+003	1000
Water	33.5	208	1000
Soil	66.5	416	1000
Sediment	0.0592	1.87e+003	0

Persistence Time: 391 hr

Appendix B

OECD QSAR Toolbox: