

HAZARDOUS MATERIALS AND WASTE MANAGEMENT DIVISION

RE: Hazardous Waste Determination for Epinephrine

DATE: August 31, 2006

In recent years, the use of dilute solutions containing epinephrine salts has significantly increased in medical applications. Dilute solutions of epinephrine salts are now widely used in local anesthetics, eye surgery applications, and orthopedic surgery applications. More concentrated solutions have been used for many years in cardiac applications and treatment of severe allergic reactions. Wastes contaminated with these epinephrine salt solutions include vials, ampules, bottles, bags, tubing, and syringes and can be generated in large amounts at a given facility.

Colorado has closely evaluated these applications, the epinephrine salts utilized, and the wastes produced from both a technical and regulatory point of view. In summary, Colorado has determined that in most, and maybe all, of the medical applications where epinephrine salt solutions are used, the epinephrine salt does **not** meet the listing description for the P042 waste (found in section 261.33 of the Colorado hazardous waste regulations, 6 CCR 1007-3). Therefore, the materials contaminated by the epinephrine salts are not hazardous waste and/or do not need to be managed as hazardous waste. These wastes are, however, solid wastes and medical wastes and still need to be managed in compliance with solid waste requirements.

Background

Pure epinephrine (or epinephrine base; CAS 51-43-4; $C_9H_{13}NO_3$) appears in the Colorado hazardous waste regulations as a P042 listed acutely hazardous waste. This form of epinephrine is a weak nitrogenous base and a secondary amine and has a low solubility in water due to the fact it has no formal charge. However, solubility increases significantly in mineral acid and sodium hydroxide and potassium hydroxide solutions as the epinephrine accepts a proton in a reversible acid-base reaction forming an aqueous hydroxyl-amine salt (protonated form; $C_9H_{14}NO_3^+$). For instance, epinephrine base will dissolve in aqueous buffer solutions at pH 7.4 with analogous salt formation and these solutions are widely used in medical applications. Many amino compounds like epinephrine are used as drugs, and these drugs are administered as their water-soluble salts rather than their water-insoluble "free base" amine form.

In other medical applications, an epinephrine salt is the listed ingredient in the solution being utilized. The most common salt in these solutions is epinephrine hydrochloride, but epinephrine bitartrate and others are also used. In these solutions, the same protonated ion is present along with a negatively charged counter ion.

Colorado has determined that epinephrine salt solutions are not P042 listed hazardous waste for the following reasons:

- 1) Epinephrine base is the specific chemical listed in the P042 hazardous waste listing. It is a completely different compound than any of the epinephrine salts. Epinephrine and epinephrine salts have different chemical and physical properties - solubilities, melting points, etc. They also have different CAS numbers. Recreating epinephrine base from its salts by the addition of strong bases like NaOH and KOH is very unlikely because that would be inconsistent with the physiological use of this drug in vivo. Likewise, recreating free base epinephrine in wastes generated from the use of epinephrine salts, without the addition of strong bases, is unlikely and improbable. Furthermore, the concentration of epinephrine salts, as employed in medical procedures, are usually on the order of picograms per milliliter (parts per trillion).
- 2) EPA has specifically listed some acutely toxic chemicals on the P-list to include the salts of those chemicals. Examples include warfarin, strychnine, nicotine, and others. Epinephrine salts are not included in the P042 listing for epinephrine in section 261.33(e). We conclude that not including epinephrine salts in the P042 listing was a deliberate decision on EPA's part.
- 3) The state of Florida asked EPA in 1998 whether the U-listing for chloral (U-034) included chloral hydrate, which has a different CAS number than chloral. EPA responded by saying both chloral and chloral hydrate were included in the U-034 listing and that the CAS number was included only as an "identification aid." This EPA response pointed out that this was consistent with a 1992 EPA letter that clarified that the U-058 listing for cyclophosphamide included cyclophosphamide monohydrate. We think both of these findings by EPA were accurate and appropriate since both of these compounds and their hydrated forms have identical chemical properties, toxicity, ionic states, etc. This, however, is not the case for epinephrine and epinephrine salt.
- 4) The most common epinephrine salt is epinephrine hydrochloride. As explained above, this is a different chemical than the P042 epinephrine base with different chemical properties. Epinephrine hydrochloride is widely manufactured for medical applications and sold in varying concentration for different uses. As such, it is a different commercial chemical product than the epinephrine base that is listed as P042. Because it is widely manufactured and sold for direct application, it is also not a manufacturing chemical intermediate.
- 5) An analogous hazardous waste listing example is beryllium powder, which carries the hazardous waste listing of P015. EPA specifically listed only beryllium powder and the listing does not include other forms of beryllium metal.

Epinephrine – Chemical Data

Chemical Formula:	C ₉ H ₁₃ NO ₃
Molecular weight:	183.3
Synonym:	Adrenaline
Appearance:	light brown to white powder
Solubility	Sparingly soluble in water. Readily soluble in mineral acids, sodium hydroxide and potassium hydroxide. ^{1,2} Combined with acids, forming water soluble salts. ²
Melting Point:	211-212°C
Boiling point	
Density	
Stability:	Stable. Incompatible with acids, acid chlorides, acid anhydrides, oxidizing agents. Light sensitive.
Toxicity:	Highly toxic. May be fatal if inhaled, swallowed or absorbed through the skin. May cause harm or be fatal to the unborn child. Note low LD50s below. May cause reproductive defects.

SCU-RAT LD50 5 mg kg⁻¹
IVN-RAT LD50 0.15 mg kg⁻¹
IPR-MUS LD50 4 mg kg⁻¹
SCU-RBT LD50 4 mg kg⁻¹
SCU-MAN LDLO 0.007 mg kg⁻¹
ORL-RAT LDLO 30 mg kg⁻¹

Epinephrine Hydrochloride – Chemical Date

Chemical Formula:	C ₉ H ₁₄ ClNO ₃
Molecular weight:	183.3
Synonym:	
Appearance:	
Solubility	Readily soluble in water.
Melting Point:	157°C
Boiling point	
Density	
Stability:	
Toxicity:	

1 Van Nostrand Reinhold Publishing, The Condensed Chemical Dictionary, Eighth Edition, p 349.

2 The Merck Index, Eleventh Edition, p 567.