

# Pamidronic Acid

sc-219549



The Power is Question

Material Safety Data Sheet

Hazard Alert Code Key: **EXTREME** **HIGH** **MODERATE** **LOW**

## Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

### PRODUCT NAME

Pamidronic Acid

### STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

### NFPA



### SUPPLIER

Santa Cruz Biotechnology, Inc.  
2145 Delaware Avenue  
Santa Cruz, California 95060  
800.457.3801 or 831.457.3800

### EMERGENCY:

ChemWatch

Within the US & Canada: 877-715-9305

Outside the US & Canada: +800 2436 2255

(1-800-CHEMCALL) or call +613 9573 3112

### SYNONYMS

C3-H11-N-O7-P2, H2NCH2CH2C(HPO4)2OH, "ADP acid", AHPPrBP, "3-amino-1-hydroxypropylidene-1, 1-bisphosphonic acid", "(3-amino-1-hydroxypropylidene)diphosphonic acid", "aminohydroxypropylidene diphosphonic acid", bisphosphonate, "calcium metabolism regulator"

## Section 2 - HAZARDS IDENTIFICATION

### CHEMWATCH HAZARD RATINGS

	Min	Max
Flammability:	1	
Toxicity:	2	
Body Contact:	2	
Reactivity:	1	
Chronic:	2	

Min/Nil=0  
Low=1  
Moderate=2  
High=3  
Extreme=4



### CANADIAN WHMIS SYMBOLS



## EMERGENCY OVERVIEW

### RISK

Harmful if swallowed.

Possible risk of harm to the unborn child.

May cause long-term adverse effects in the aquatic environment.

### POTENTIAL HEALTH EFFECTS

#### ACUTE HEALTH EFFECTS

##### SWALLOWED

■ Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

■ Adverse effects produced by bisphosphonate therapy may include black or tarry stools; jaw pain; eye inflammation, pain, or vision change; low levels of calcium in the blood (may cause confusion, severe fatigue or weakness); pain or difficulty when swallowing; skin rash or itching; swelling of the lips, face, tongue, or throat; bone, muscle, or joint pain; diarrhea or constipation; headache; indigestion or stomach gas; stomach pain; and nausea.

Possible allergic reaction to material if inhaled, ingested, or in contact with skin.

##### EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn).

Slight abrasive damage may also result.

##### SKIN

■ Skin contact is not thought to produce harmful health effects (as classified using animal models).

Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects.

Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

##### INHALED

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

■ The material can cause respiratory irritation in some persons.

The body's response to such irritation can cause further lung damage.

#### CHRONIC HEALTH EFFECTS

■ Results in experiments suggest that this material may cause disorders in the development of the embryo or fetus, even when no signs of poisoning show in the mother.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

There is some evidence that inhaling this product is more likely to cause a sensitization reaction in some persons compared to the general population.

There is limited evidence that, skin contact with this product is more likely to cause a sensitization reaction in some persons compared to the general population.

Exposure to small quantities may induce hypersensitivity reactions characterized by acute bronchospasm, hives (urticaria), deep dermal wheals (angioneurotic edema), running nose (rhinitis) and blurred vision . Anaphylactic shock and skin rash (non-thrombocytopenic purpura) may occur.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

Respiratory sensitization may result in allergic/asthma like responses; from coughing and minor breathing difficulties to bronchitis with wheezing, gasping.

Prolonged use may produce hypocalcaemia, a susceptibility to fracture bones, anaemia, kidney damage, and gastrointestinal irritation with ulceration. Although the material has not been subjected to controlled pregnancy studies in humans, animal experiments have produced birth abnormalities.

## Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
pamidronic acid	40391-99-9	>98

## Section 4 - FIRST AID MEASURES

### SWALLOWED

· IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY. · Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:

### EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

### SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

### INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

### NOTES TO PHYSICIAN

■ Treatment of bisphosphonate overdose should be symptomatic and supportive and may include the following:

- Administer activated charcoal as a slurry.
- Perform gastric lavage soon after ingestion (within one hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
- Monitor vital signs frequently and perform continuous ECG monitoring.
- For hypocalcaemia, treat with intravenous calcium salts. More rapid administration may be necessary.
- Monitor patients for signs and symptoms of upper gastrointestinal ulcerations and/or hemorrhage.
- For torsades de pointes, haemodynamically unstable patients may need electrical cardioversion. Treat stable patients with magnesium, isoproterenol, and/or atrial overdrive pacing. Correct electrolyte imbalances.
- Administer a benzodiazepine for seizures. Consider phenobarbital if seizures recur. Monitor for hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation. Evaluate for hypoglycemia, electrolyte disturbances, and hypoxia.
- Antacids may be used to treat gastrointestinal symptoms.

Meditext 2008

Hypersensitivity (anaphylactic) reactions should receive immediate medical attention.

Medical conditions aggravated by exposure:

Impaired kidney function, a tendency to fracture bones, hyperphosphataemia, hypocalcaemia, hypovitaminosis D.

Treat symptomatically.

Pamidronic acid is not well absorbed from the gastrointestinal tract.

## Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available

### EXTINGUISHING MEDIA

- Foam.
- Dry chemical powder.

### FIRE FIGHTING

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.

### GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO<sub>2</sub>), nitrogen oxides (NO<sub>x</sub>), phosphorus oxides (PO<sub>x</sub>), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

May emit corrosive fumes.

### FIRE INCOMPATIBILITY

■ Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

### PERSONAL PROTECTION

Glasses:

Safety Glasses.

Chemical goggles.

Gloves:

Respirator:

Particulate

## Section 6 - ACCIDENTAL RELEASE MEASURES

### MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

### MAJOR SPILLS

- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.

## Section 7 - HANDLING AND STORAGE

### PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
  - Wear protective clothing when risk of exposure occurs.
- Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
- Do NOT cut, drill, grind or weld such containers.
  - In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

### RECOMMENDED STORAGE METHODS

- Glass container.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

### STORAGE REQUIREMENTS

- Observe manufacturer's storing and handling recommendations.

## Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

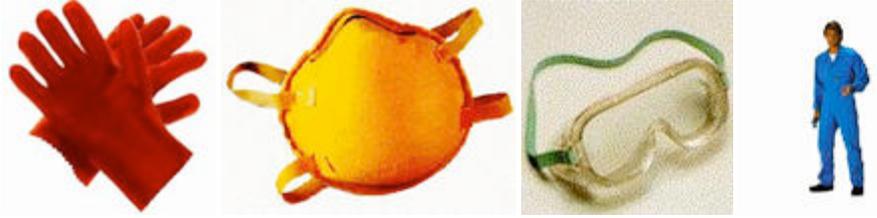
### EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m <sup>3</sup>	STEL ppm	STEL mg/m <sup>3</sup>	Peak ppm	Peak mg/m <sup>3</sup>	TWA F/CC	Notes
Canada - Ontario Occupational Exposure Limits	pamidronic acid (Particles (Insoluble or Poorly Soluble) Not Otherwise)		10 (I)						
Canada - British Columbia Occupational Exposure Limits	pamidronic acid (Particles (Insoluble or Poorly Soluble) Not Otherwise Classified (PNOC))		10 (N)						
Canada - Ontario Occupational Exposure Limits	pamidronic acid (Specified (PNOS) / Particules (insolubles ou peu solubles) non précisées par ailleurs)		3 (R)						

US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	pamidronic acid (Particulates not otherwise regulated Respirable fraction)	5	
US - California Permissible Exposure Limits for Chemical Contaminants	pamidronic acid (Particulates not otherwise regulated Respirable fraction)	5	(n)
US - Oregon Permissible Exposure Limits (Z-1)	pamidronic acid (Particulates not otherwise regulated (PNOR) (f) Total Dust)	10	Bold print identifies substances for which the Oregon Permissible Exposure Limits (PELs) are different than the federal Limits. PNOR means "particles not otherwise regulated."
US - Michigan Exposure Limits for Air Contaminants	pamidronic acid (Particulates not otherwise regulated, Respirable dust)	5	
US - Oregon Permissible Exposure Limits (Z-1)	pamidronic acid (Particulates not otherwise regulated (PNOR) (f) Respirable Fraction)	5	Bold print identifies substances for which the Oregon Permissible Exposure Limits (PELs) are different than the federal Limits. PNOR means "particles not otherwise regulated."
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	pamidronic acid (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)	5	
Canada - Prince Edward Island Occupational Exposure Limits	pamidronic acid (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)	10	See Appendix B current TLV/BEI Book

ENDOELTABLE

**PERSONAL PROTECTION**



## RESPIRATOR

•Particulate. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

## EYE

■ When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent].

## HANDS/FEET

■ NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.

Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers. [AS/NZS 2210]
- Head covering.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

## OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit.

## ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

# Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

## PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	235.07
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not available.	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

## APPEARANCE

White, odourless, crystalline powder; does not mix well with water (0.3%).

## Section 10 - CHEMICAL STABILITY

### CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.

### STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

## Section 11 - TOXICOLOGICAL INFORMATION

pamidronic acid

### TOXICITY AND IRRITATION

PAMIDRONIC ACID:

- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY	IRRITATION
Oral (rat) LD50: 1510 mg/kg *	Nil Reported

Intraperitoneal (mouse) LD50: 118 m/kg \*\* [Gador S.A.]

■ Oral bisphosphonates (given in certain medical treatments) can give stomach upset and inflammation and erosions of the esophagus, which is the main problem of oral N-containing preparations. This can be prevented by remaining seated upright for 30 to 60 minutes after taking the medication. Intravenous bisphosphonates can give fever and flu-like symptoms after the first infusion, which is thought to occur because of their potential to activate human T cells. Notably, these symptoms do not recur with subsequent infusions. There is a slightly increased risk for electrolyte disturbances, but not enough to warrant regular monitoring. In chronic renal failure, the drugs are excreted much slower, and dose adjustment is required. Bisphosphonates have been associated with osteonecrosis of the jaw; with the mandible twice as frequently affected as the maxilla and most cases occurring following high-dose intravenous administration used for some cancer patients. Some 60% of cases are preceded by a dental surgical procedure and it has been suggested that bisphosphonate treatment should be postponed until after any dental work to eliminate potential sites of infection. A number of cases of severe bone, joint, or musculoskeletal pain have been reported, prompting labeling changes.

Bisphosphonates are incorporated into the bone matrix, from where they are gradually released over periods of weeks to years. The extent of bisphosphonate incorporation into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the total dose and duration of bisphosphonate use. Although there are no data on foetal risk in humans, bisphosphonates do cause foetal harm in animals, and animal data suggest that uptake of bisphosphonates into foetal bone is greater than into maternal bone. Therefore, there is a theoretical risk of foetal harm (e.g., skeletal and other abnormalities) if a woman becomes pregnant after completing a course of bisphosphonate therapy. The impact of variables such as time between cessation of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of administration (intravenous versus oral) on this risk has not been established.

The non-nitrogenous bisphosphonates (disphosphonates) are metabolised in the cell to compounds that compete with adenosine triphosphate (ATP) in the cellular energy metabolism. The osteoclast initiates apoptosis and dies, leading to an overall decrease in the breakdown of bone.

Nitrogenous bisphosphonates act on bone metabolism by binding and blocking the enzyme farnesyl diphosphate synthase (FPPS) in the HMG-CoA reductase pathway (also known as the mevalonate pathway). Disruption of the HMG CoA-reductase pathway at the level of FPPS prevents the formation of two metabolites (farnesol and geranylgeraniol) that are essential for connecting some small proteins to the cell membrane. This phenomenon is known as prenylation, and is important for proper sub-cellular protein trafficking.

The material may be irritating to the eye, with prolonged contact causing inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis.

Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

The material may produce respiratory tract irritation, and result in damage to the lung including reduced lung function.

The material may cause skin irritation after prolonged or repeated exposure and may produce on contact skin redness, swelling, the production of vesicles, scaling and thickening of the skin.

for disodium salt

Visual field changes, diplopia, effects on newborn, foetotoxicity, specific developmental abnormalities (musculoskeletal system) recorded.

## Section 12 - ECOLOGICAL INFORMATION

May cause long-term adverse effects in the aquatic environment.

### Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
pamidronic acid	HIGH	No Data Available	LOW	HIGH

## Section 13 - DISPOSAL CONSIDERATIONS

### Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

‡ Puncture containers to prevent re-use and bury at an authorized landfill.

Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

## Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

## Section 15 - REGULATORY INFORMATION

**pamidronic acid (CAS: 40391-99-9) is found on the following regulatory lists;**

"US - California Air Toxics ""Hot Spots"" List (Assembly Bill 2588) Substances for which emissions must be quantified"

## Section 16 - OTHER INFORMATION

### LIMITED EVIDENCE

- Cumulative effects may result following exposure\*.

- May produce discomfort of the respiratory system\*.
  - Possible respiratory and skin sensitiser\*.
- \* (limited evidence).

### **Denmark Advisory list for selfclassification of dangerous substances**

Substance CAS Suggested codes pamidronic acid 40391- 99- 9 Xn; R22

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- Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:  
[www.chemwatch.net/references](http://www.chemwatch.net/references).

- The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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Issue Date: Jan-24-2011

Print Date: Jul-27-2011