RJA 2/17/22
JS 2/22/22

[redacted]

P-18-0233

Chemical Name: [redacted]

CASRN: [redacted]

ASSIGNMENTS	NAME	DATE
SAT Chair	[redacted]	07-17-2018
HH Hazard Assessor (A)	[redacted]	07-17-2018
HH Hazard QC Reviewer (A)	[redacted]	07-20-2018
HH Risk Assessor FOCUS (B)	[redacted]	08-06-2018
HH Risk QC Reviewer (B)	[redacted]	08-03-2018

Human Health Report Status:		DATE COMPLETED
X	HAZARD DRAFT- Pending Review	07-17-2018
X	HAZARD REVIEWED	07-20-2018
X	HAZARD FINAL	07-23-2018
X	RISK DRAFT- Pending Review	08-03-2018
X	RISK REVIEWED	08-03-2018
X	RISK-FOCUS FINAL- Uploaded	10-15-2018
X	POST-FOCUS UPDATE DRAFT	11-01-2018
X	POST-FOCUS UPDATE FINAL- Uploaded	11-02-2018

1 HUMAN HEALTH SUMMARY

EPA estimated the human health hazard of this chemical substance based on its estimated physical/chemical properties, and by comparing it to structurally analogous chemical substances for which there is information on human health hazard. EPA concludes there is moderate concern for human health hazard for the chemical substance.

Based on the hazard determination and available quantitative and qualitative risk information, EPA concludes that there is risk for the PMN substance. The risk estimates for this chemical are for the intended and reasonably foreseen conditions of use, as well as for a hypothetical consumer scenario that is not considered reasonably foreseen. Other conditions of use and their risks were not evaluated.

1.1 Hazard Summary

- Absorption of the neat material is nil all routes; if in solution, absorption of the [redacted] fractions is poor all routes (pchem).
- Potential concern for lung toxicity based on cationic binding (uncertainty based on [redacted] FGEW for amines).
- Concerns for systemic, reproductive and developmental toxicity if dimethylethanolamine (DMEA) and ethylene glycol are released from the absorbed [redacted] fractions.

1.2 Risk Summary

1.2.1 Workers

Risks were not identified for systemic (stomach ulcerations) or reproductive toxicity (increased post-implantation loss) via dermal or inhalation exposure based on quantitative analogue data for DMEA, a LMW component (5%) of the PMN (MOE's = 2000 and 16,000 for dermal and inhalation exposure, respectively; benchmark MOE = 1000).

Although concern for lung effects via inhalation based on polycationic binding was identified for workers, these effects are unlikely given the high FGEW for amines (i.e., only two cationic amines expected per molecule), large molecular weight, and steric hindrance associated with this PMN.

1.2.2 General Population

Risks were not identified for systemic (stomach ulcerations) or reproductive toxicity (increased post-implantation loss) via drinking water exposure based on quantitative hazard data for DMEA, a LMW component (5%) of the PMN (MOE's = 3.3E+5 and 7.9E+4 for adults and children, respectively; benchmark MOE = 100).

1.2.3 Consumers

Risks were not identified for systemic (stomach ulcerations) or reproductive toxicity (increased post-implantation loss) via dermal or inhalation exposure based on quantitative hazard data for

[redacted]

DMEA, a LMW component (5%) of the PMN (MOEs = 1,800 and 11,000 for dermal and inhalation exposure, respectively; benchmark MOE = 100).

Although potential for lung effects were identified via inhalation based on polycationic binding, these effects are unlikely given the [redacted] FGEW for amines (i.e., only two cationic amines expected per molecule), large molecular weight and steric hindrance associated with this PMN.

1.3 Potentially Useful Information:

1.3.1 Assumptions and Uncertainties

Absorption of the PMN is based on p-chem properties.
There are no measured data on the PMN substance itself.
Health effects are based on structural alerts and metabolites.
The evaluation of the PMN is based on presumed metabolite.

1.3.2 Potentially Useful Information

Potentially useful information would inform understanding of:
Absorption and metabolism;
Systemic, reproductive, and developmental toxicities.

[redacted]

2 HUMAN HEALTH HAZARD- PART A

2.1 Chemistry Summary

PMN: P-18-0233	Submitter: [redacted]				Manu.	Import
Max. PV (KG):	[redacted]	Binding Option Marked:				X
MW: [redacted]	[redacted]	% < 500	[redacted]	% <1000	CASNC [redacted]	

[redacted]	Prop.	Meas.	Est.
	MP		
	BP		[redacted]
	Pres.		at 760 mm Hg
	VP		<0.000001
	S-H2C		<0.000001
	log P		

[redacted]	Analogs: [redacted]
USE: [redacted]	[redacted]

2.1 SAT Summary

2.1.1 PMN Health Rating

2

2.1.2 SAT Key Words

SYSTEMIC TOXICITY, REPRODUCTIVE TOXICITY, DEVELOPMENTAL TOXICITY

2.1.3 Absorption

Absorption of the neat material is nil all routes; if in solution absorption of the [redacted] fractions is poor all routes (pchem).

[redacted]

2.1.4 SAT Health Summary

There is potential concern for lung toxicity based on cationic binding (uncertainty based on high FGEW for amines; i.e. [redacted]). If DMEA and ethylene glycol are released from the absorbed [redacted] fractions, there are concerns for systemic, reproductive and developmental toxicity.

2.1.5 PMN Data (Study summary, POD)

No PMN data submitted.

2.1.6 Analog Data (analog, structure, study summary, POD)

CHEMISTRY REPORT ver. 04/98	PAGE 5	PMN: P-18-0233	
(38) ANALOGS:			
PMN or CAS No.	Chem. Name	Structure	TSCA Y/N
[redacted]			

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

2.1.7 Other Information (SDS, structural alert or component of interest, basis, etc.)

SDS: mixture

[redacted]

- [redacted]

- [redacted]
  - [redacted]
  - [redacted]

- [redacted]
  - [redacted]

[redacted]1

- [redacted]

Cationic Binding

According to RAD's Lung Toxicity Project, the POD for cationic binding is 1.6 mg/m^3, which is the LOAEC identified in a study on polyhexamethylene guanidine phosphate (Kim et al., 2016). Note, this POD is likely to be too conservative since the FGEW=1700 and the MW of 3400 suggests that only 2 amine groups/molecule for this substance and the recommended POD substance has many amine groups per molecule.

2.1.8 Exposure Routes of Interest

[	Route of Interest
x	Inhalation:
x	Dermal:
x	Ingestion:

2.2 Human Health Category (From US EPA 2010 document)

Chemical Category: N/A
Chemical Category Health Concerns:
Category Testing Strategy:

2.3 Point of Departure Selected and Basis

2.3.1 POD for [redacted]) for inhalation exposures

POD type: [redacted]
POD Value: [redacted]
POD Chemical: [redacted]
POD Route: [redacted]
POD Hazard Endpoint: [redacted]
POD Basis: [redacted]
POD Benchmark MOE: [redacted]
Reference: [redacted]

[redacted]

2.3.2 POD for [redacted] for oral exposures

POD type: [redacted]
POD Value: [redacted]
POD Chemical: [redacted]
POD Route: [redacted]
POD Hazard Endpoint [redacted]
POD Basis: [redacted]
POD Benchmark MOE: [redacted]
Reference: [redacted]

2.3.3 POD for [redacted] for oral exposures

POD type: [redacted]
POD Value: [redacted]
POD Chemical: [redacted]
POD Route: [redacted]
POD Hazard Endpoint: [redacted]
POD Basis [redacted]
POD Benchmark MOE: [redacted]
Reference: . [redacted]

[redacted]

3 HUMAN HEALTH RISK (PART B)

3.1 USES and EXPOSURES

3.1.1 Uses

Resin in solvent-borne [redacted].

3.1.2 Worker Exposure

3.1.2.1 Inhalation

[redacted] (particulate; non-volatile) Submitter provided information on droplet size that indicates 0.2% of aerosol is within the respirable range (<10 µm).

3.1.2.2 Dermal

[redacted]

3.1.3 General Population Exposure

Exposure Scenario[1]	Water						Landfill	Stack Air		Fugitive Air	
Release activity(ies)[2]; exposure calculation(s)[3]	Drinking Water		Fish Ingestion		7Q10[4] CC = N/A	PDM Days Exceeded	LADD	ADR (24-hr conc.)	LADD (Annual conc.)	ADR (24-hr conc.)	LADD (Annual conc.)
	ADR	LADD	ADR	LADD							
	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	µg/l	# Days	mg/kg/day	mg/kg/day (µg/m^3)	mg/kg/day (µg/m^3)	mg/kg/day (µg/m^3)	mg/kg/day (µg/m^3)
PROC:Max ADR	**1.82E-2**	--	--	--	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)
PROC:Max LADD	--	**2.55E-5**	--	--	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)
USE:Max ADR	**6.55E-6**	--	--	--	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)
USE:Max LADD	--	**3.68E-8**	--	--	--	--	--	-- (--)	-- (--)	-- (--)	-- (--)

3.1.3.1 Drinking Water

0.0182 mg/kg/d

3.1.3.2 Fish

Not evaluated based on no releases to water.

3.1.3.3 Air/Inhalation

Below modeling thresholds.

3.1.4 Consumer Exposure

At the time the PMN was originally submitted, consumer use, and thus, consumer exposure, were reasonably foreseen due to the proposed use of the PMN in coatings. While it is important to note that these hypothetical exposures are not associated with unreasonable risk (see Section 3.2.3), updates made to the *TSCA New Chemicals Review Framework for Identifying Reasonably Foreseen Conditions of Use* after the generation of these hypothetical exposures resulted in this PMN no longer being expected to have consumer uses. The information included here is for purposes of transparency and completeness only.

[redacted]

Scenario	Water (DtD)						Dermal		Inhalation	
	Drinking Water		Fish Ingestion		7Q10	PDM Days Exceeded	ADR	LADD	ADR	LADD
	ADR	LADD	ADR	LADD						
	mg/kg/ day	mg/kg/ day	mg/kg /day	mg/kg/ day	µg/l	# Days	mg/kg/ day	mg/kg/ day	mg/kg/ day	mg/kg/ day
CEM[2], Aerosol Paint	---	---	---	---	---	---	---	---	**1.22E-02**	**3.13E-04**
CEM[2], Latex Paint	---	---	---	---	---	---	**1.12E+01**	**1.74E-02**	**3.36E-02**	**2.96E-03**

3.1.4.1 Dermal

11.2 mg/kg/d

3.1.4.2 Inhalation

0.0336 mg/kg/d

3.2 RISK CALCULATIONS

3.2.1 Worker Calculations

Worker Margin of Exposure (MOE) Calculations using Animal Oral POD and Engineering Report PDR

	Animal or Human POD			Worker Exposure				Human Breathing Rates						Benchmark MOE	Endpoint Type
Exposure Route	POD Conc. mg/m³	POD Period hrs/day	POD Duration days/wk	Exposure mg/day Potential Dose Rate (PDR)	Total Worker Breathing Volume for PDR Exposure Period m³	Worker Exposure Duration Hours/Day	Exposure Duration Days/Wk	Default	Worker	Structural Alert as % of PMN	POD Conc - Duration & Breathing Rate Correction Scenario$_{HEC}$ mg/m³	Exposure TWA mg/m³	**Margin of Exposure MOE**	100	NOAEL
Inhalation	3.6E+01	6.00	5	[redacted]	10.0	[redacted]	[redacted]	4.90	10.00	5%	1.3E+01	3.0E+00	**8.9E+01**	Fold Factor =	1.1

Worker Margin of Exposure (MOE) Calculations using Animal Oral POD and Engineering Report PDR

	Animal or Human			Human							Benchmark MOE	Endpoint Type
Exposure Route	POD mg/kg-day	POD Exposure Duration Days/Wk	POD Route % Absorp	Exposure mg/day Potential Dose Rate (PDR)	Exposure Duration Days/Wk	Exposure Route % Absorp	Body Weight kg	Exposure mg/kg-day	Structural Alert as % of PMN	Margin of Exposure MOE	1000	LOAEL
Dermal	3.0E+02	5	100%	[redacted]	[redacted]	0.15%	80	2.0E+01	5%	**200000.0**	[redacted]	

Worker risks were not identified for developmental toxicity (increased post-implantation loss) via dermal exposure based on quantitative analogue data for a structural component of the PMN (MOE_{dermal} = 200,000; Benchmark MOE = 1000). Worker risks were identified for inhalation exposure based on quantitative analogue data for a structural component of the PMN (MOE = 89; benchmark MOE = 100).

[redacted]

Worker Margin of Exposure (MOE) Calculations using Animal Oral POD and Engineering Report PDR															
	Animal or Human POD			Worker Exposure				Human Breathing Rates						Benchmark MOE	Endpoint Type
Exposure Route	POD Conc. mg/m³	POD Period hrs/day	POD Duration days/wk	Exposure mg/day Potential Dose Rate (PDR)	Total Worker Breathing Volume for PDR Exposure Period m³	Worker Exposure Duration Hours/Day	Exposure Duration Days/Wk	Default	Worker	Structural Alert as % of PMN	POD Conc - Duration & Breathing Rate Correction Scenario$_{HEC}$ mg/m³	Exposure TWA mg/m³	**Margin of Exposure MOE**	100	NOAEL
Inhalation	3.6E+01	6.00	5	[redacted]	10.0	[redacted]	[redacted]	4.90	10.00	5%	1.3E+01	3.0E+00	**8.9E+01**	Fold Factor =	1.1

Worker risks were identified for maternal toxicity via inhalation exposure based on quantitative analog data for a structural component of the PMN (MOE =89; Benchmark MOE = 100).

3.2.2 General Population Calculations

Focus General Population and Consumer MOE Calculations MOE = (POD x Abs Rate) / ((PDR x Abs Rate) / BW) Benchmark (acceptable) MOE ≥100																
Exposure Scenarios and Values[1]		POD= NOAEL (mg/kg/day)		POD Route Absorp Adj[2]				Exposure Acute Dose Rate (mg/kg/day)		Exposure Route Absorp Adj[2]		Multiplier for Sensitive Sub-populations[4]		Structural Alert/ Component as % of PMN		Margin of Exposure (POD/PMN Dose)
GENERAL POPULATION RISK																(NOAEL=100)
Highest/Worst Case Doses from Exposure Report																
Drinking Water	(	300	x	100%	)	÷	(	1.82E-02	x	100%	x	1.00	x	5%	) =	329670
Drinking Water	(	300	x	100%	)	÷	(	1.82E-02	x	100%	x	4.17	x	5%	) =	79058

[1] General Population and Consumer ingestion Acute Dose Rates are from the Exposure Report and are generated using E-FAST which assumes a 100% absorption rate, and uses an average adult body weight of 80 kg. Consumer ADRs are generated using the Consumer Exposure Module within the E-FAST CBI version called "NCEM2" model.

[2] Absorption adjustments for Focus: Assume 100% POD; if risks, consider adjusting for absorption, etc.

[3] Benchmark (Acceptable) MOEs are 100 for NOAEL-based assessment and 1000 for LOAEL-based assessment.

[4] Multiplier based on increased drinking water consumption for infants. Multiplier would be less for older populations, so this value is worst-case.

Risks to the general population for systemic or repro/developmental toxicity via drinking water ingestion were not identified.

3.2.3 Consumer Calculations

Exposure Route	POD mg/kg-day	POD Exposure Duration Days/Wk	POD Route % Absorp	Exposure mg/day Potential Dose Rate (PDR)	Exposure Duration Days/Wk	Exposure Route % Absorp	Body Weight kg	Exposure mg/kg-day	Structural Alert as % of PMN	Margin of Exposure MOE	100	NOAEL
Dermal	3.0E+02	5	100%	[redacted]	[redacted]	15%	80	1.1E+01	5%	**145454.5**	[redacted]	

Population/Consumer Margin of Exposure (MOE) Calculations using Animal Oral POD and Engineering Report PDR											
	Animal or Human POD			Population Exposure						Benchmark MOE	Endpoint Type
Inhalation Exposure Scenario	POD Conc. mg/m³	POD Period hrs/day	POD Duration days/wk	Exposure (24-hr conc.) (ug/m3)	Population Exposure Duration Hours/Day	Exposure Duration Days/Wk	Structural Alert as % of PMN	POD Conc - Duration Correction - Scenario$_{HEC}$ mg/m³	**Margin of Exposure MOE**	1000	LOAEL
Latex Paint	3.6E+01	6.00	[redacted]	3.4E-02	[redacted]	[redacted]	100%	9.1E+00	**2.7E+05**	[redacted]	

Risks to consumers for systemic or repro/developmental toxicity via dermal or inhalation exposure were not identified.