[redacted]

P-20-0168

Chemical Name: [redacted]

[redacted]

CASRN: [redacted]

Human Health Report Status:	DATE COMPLETED
HAZARD DRAFT- Pending Review	09-23-2020
HAZARD REVIEWED	09-24-2020
RISK DRAFT- Pending review	10-13-2020
RISK QC	10-14-2020
RISK REVIEWED	01-14-2021
RISK FINAL- Uploaded	01-14-2021
UPDATE DRAFT – Pending review	
UPDATE REVIEWED	
UPDATE FINAL- Uploaded	

[redacted]

1 HUMAN HEALTH SUMMARY

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

1.1 Hazard 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. Absorption of the parent polymer is expected to be nil through the skin, gastrointestinal (GI) tract, and lungs based on physical/chemical properties. Absorption of the low molecular weight fraction (0.43% < 500 Daltons, 3.41% < 1000 Daltons) is expected to be poor to moderate through the skin, moderate through the GI tract, and poor through the lungs based on physical/chemical properties. For the new chemical substance, EPA identified hazards for irritation to eyes, skin, and respiratory tract based on the structural alert for [redacted] and test data on analogues [redacted]. Submitted tests on analogues of the new chemical substance reported one analogue [redacted] as not acutely toxic in oral and dermal tests in rats (OECD 401, OECD 402, and OECD non-guideline), irritating to skin and eyes in rabbits (OECD 404, OECD 405, and OECD non-guideline), non-sensitizing in guinea pigs (OECD non-guideline), negative for mutagenicity in bacteria (OECD 471), negative for chromosome aberrations in vitro (OECD non-guideline), and did not identify adverse effects in a 28-day repeated-dose oral study in rats; dermal irritation was observed in a 28-day dermal study in rats, with no adverse systemic effects (OECD non-guideline). Submitted test on a second analogue [redacted] reported the test substance as not acutely toxic in oral and dermal tests in rats (OECD 423, OECD 402), irritating to skin and eyes in rabbits (OECD 404, OECD 405), non-sensitizing in guinea pigs (OECD 406), negative for mutagenicity in bacteria (OECD 471), negative for chromosomal aberrations in vitro (OECD 473), negative for induction of micronuclei in vivo in mice (OECD 474), and did not identify effects in a 14-day repeated-dose oral study in rats (OECD non-guideline) or in a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (OECD 422). EPA qualitatively evaluated irritation effects.

1.2 Exposure and Risk Summary

For this assessment, EPA assessed worker exposure via dermal exposure. Inhalation exposures to workers are not expected. Releases to air and landfill were estimated. No releases to water were expected. Exposures to the general population were not assessed because exposures are not expected. Exposure to consumers was assessed via dermal exposures.

Based on the hazard determination and available qualitative risk information, EPA did not identify risks for the new chemical substance.

[redacted]

1.2.1 Workers

Irritation hazards to workers via dermal contact were identified based on the structural alert for [redacted] and test data on analogues. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However, exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including impervious gloves and eye protection. EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet prepared by the submitter, in a manner adequate to protect them.

No relevant systemic hazards were identified for the new chemical substance via the dermal route; therefore, risks were not calculated. Based on no identified hazards, risks are not expected.

Risks were not evaluated for workers via inhalation exposure because exposures are expected to be negligible.

1.2.2 General Population

Risks were not evaluated because general population exposures are not expected.

1.2.3 Consumers

Irritation hazards to consumers via dermal contact were identified based on test data on analogues. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

No relevant systemic hazards were identified for the new chemical substance via the dermal route; therefore, risks were not calculated. Based on no identified hazards, risks are not expected.

1.3 Assumptions and Uncertainties

- There are no measured data on the new chemical substance.
- Absorption of the new chemical substance is based on physical/chemical properties.
- Health effects and the health evaluation are based on analogue data and structure.

1.4 Potentially Useful Information

- Skin Irritation

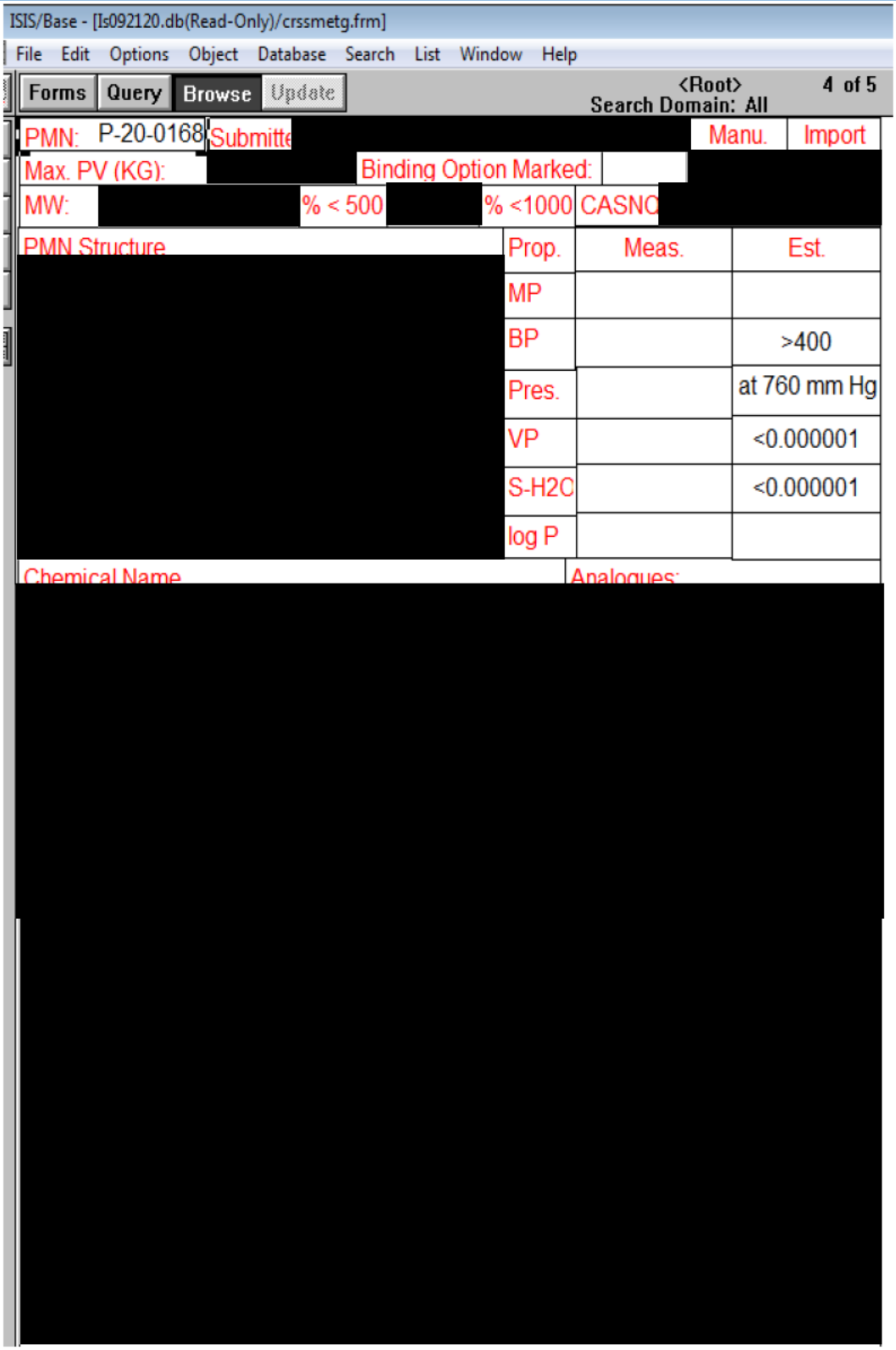
1.5 Hazard Language

Skin Irritation, Eye Irritation

[redacted]

2 HUMAN HEALTH HAZARD

2.1 Chemistry Summary



[redacted]

2.2 Hazard Summary

2.2.1 Absorption

Absorption of the parent polymer is expected to be nil through the skin, GI tract, and lungs based on physical/chemical properties.

Absorption of the low molecular weight fraction ([redacted] < 500 Daltons, [redacted] < 1000 Daltons) is expected to be poor to moderate through the skin, moderate through GI tract, and poor through the lungs, based on physical/chemical properties.

2.2.2 Structural Alerts

[redacted]

2.2.3 Human Health Category (From US EPA 2010 document)

Chemical Category: N/A for human health
Chemical Category Health Concerns: N/A
Category Testing Strategy: N/A

2.2.4 OECD QSAR Toolbox

The new chemical substance was not analyzed using the OECD QSAR Toolbox because it is outside the domain of applicability of the software.

2.2.5 Hazard Meeting Summary

The concerns for lung toxicity (cationic binding based on the polyamines and the structural alert for [redacted] are reduced based on the low content of amines and high [redacted] FGEW ([redacted] FGEW = [redacted]). Although used as a dispersant, there are no concerns for surfactancy based on structure including a lack of mixture of both hydrophobic and hydrophilic regions and no available data on surface tension or critical micelle concentration (CMC).

The concerns for blood, liver, kidney, and developmental effects based on the structural alert for nitrogen-containing heterocycles, and the concern for acute toxicity based on the structural alert for imides, are reduced based on analogue data, which showed no adverse effects up to

[redacted]
the limit dose in repeated-dose and reproductive/developmental studies [redacted].

There are concerns for irritation to eyes, skin, and respiratory tract based on the structural alert for [redacted] and test data on analogues [redacted].

2.3 Toxicity Data

2.3.1 New Chemical Substance Data

None

2.3.2 Analogue/Metabolite Data

2.3.2.1 [redacted]

Submitted analogue for [redacted]

- OECD Not Specified (reported to be similar to OECD 401): LD50 (rat) > 5000 mg/kg-bw
- OECD 401 (Acute Oral Toxicity): LD50 (rat) > 5000 mg/kg-bw
- OECD 402 (Acute Dermal Toxicity): LD50 (rat) > 2000 mg/kg-bw
- OECD Not Specified (reported to be similar to OECD 402): LD50 > 5000 mg/kg-bw; irritating to skin
- OECD 404 (Acute Dermal Irritation/Corrosion): Slightly irritating in rabbits
- OECD Not Specified (Dermal irritation): Minimally to slightly irritating in rabbits [test item is OLOA 374A based on submitted Toxicology Assessment]
- OECD Not Specified (Dermal irritation): Slight, transient irritation in rabbits (PII 0.04)
- OECD Not Specified (Eye irritation): Irritating in rabbits (24-72 hr scores iritis 0.0; redness 1.4; chemosis 0.3) [test item synonym OLOA 374A, based on submitted Toxicology Assessment]
- OECD 405 (Acute Eye Irritation/Corrosion): Irritating in rabbits (subsided by day 7)
- OECD Not Specified (Eye irritation): Transient, minor eye irritation in rabbits
- OECD Not Specified (reported to be similar to OECD 406): Not sensitizing in guinea pigs
- OECD Not Specified (reported to be similar to OECD 406): Not sensitizing in guinea pigs (positive 1/20)
- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation

[redacted]

- OECD Not Specified (reported to be similar to OECD 473): Negative in chromosomal aberration test in CHO cells
- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation
- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation
- Japanese Guideline Repeat Dose Oral (gavage) Toxicity (OECD Not Specified): Sprague-Dawley CFY rats (5/sex/group) were administered the test item via gavage at 0, 50, 250, or 1000 mg/kg-bw/day for 28 days. Additional satellite groups (5/sex/group) received the control or high-dose treatment followed by a 14-day recovery period. No treatment-related mortalities or clinical signs were observed. One male treated at 50 mg/kg-bw/day showed signs of ill health and died on day 17. This was considered incidental and not related to treatment. No effects on body weight, food consumption, or water consumption were observed. Low food consumption on day 27 was due to overnight fasting during urine collection and prior to blood sampling. No treatment-related effects on hematology were noted. Statistically significant differences were noted between low/intermediate dose animals and controls; however there was no dose-related response. Increased total bilirubin levels were noted in high-dose males and females, but direct (conjugated) bilirubin levels remained consistent between groups. Slightly elevated aspartate aminotransferase was noted in intermediate- and high-dose males, but were within the normal range for the age and strain of animals used in the study. No treatment-related effects were observed on alkaline phosphatase and aspartate aminotransferase. Calcium levels were reduced in all treated females and in intermediate- and high-dose males. This was not considered to be treatment-related and was not associated with evidence of microscopic renal damage or other blood chemistry changes such as phosphate retention or inability to retain Na+ or Cl-. All other statistically significant blood chemistry findings were within normal range for the age and strain of animals used in the study and showed no dose response. No significant differences were noted between the satellite control and high dose groups. No appreciable differences were noted in urine samples between controls and treated groups. A red appearance of the cervical lymph nodes, apparent hepatomegally and a dark appearance in the auricles of the heart were noted in the deceased low-dose animal. No other macroscopic abnormalities were noted. Increased ovary weights were noted in satellite high-dose females compared to controls, but was considered unrelated to treatment and likely cyclical in nature. No other effects on organ weights were noted. No treatment-related histopathological findings were noted. Based on the results, the 28-day NOEL was 250 mg/kg-bw/day based on increased serum bilirubin levels at 1000 mg/kg-bw/day; the biological significance of this finding was considered uncertain due to the absence of liver damage or hemolytic effects.
- A 28-day Repeat Dose Dermal Toxicity Study in rats (OECD Not Specified): Sprague-Dawley CrlCD (SD)BR rats (12/sex/group) were administered the test item via the dermal route at 0%, 3%, 15%, or 50% for six hours/day, 5 days/week for 4 weeks. No

[redacted]

mortalities or signs of toxicity were observed. Chromdacryorrhea and chromorhinorrhea noted in most animals and sores and scabs noted on the throats of 6 males across different treatment groups were all attributed to the plastic collars used to ensure the animals did not ingest the test item. Swelling of the head or face was observed in 10 animals in both sexes and across treatment groups; this finding disappeared upon removal of the collar. Swollen eyes lasting for one or two days were observed in 9 animals across sexes and treatment groups, but were only observed on weekends and in the absence of other signs. Colorless ocular discharge was observed in two animals on one day. Slow pupil response was observed in one female (treatment group not specified) during the second week of dosing, but showed normal pupil in the preceding and following weeks. Slight to severe erythema with no to slight edema was seen in control, low and mid-dose groups. Slight to severe erythema with no to well-defined edema was observed in the high-dose groups. Higher dose groups showed higher incidences of irritation at Days 2, 16, and 23 and calculated over the entire treatment period; however, there was no consistent relationship between dose and irritation. Small scabs (single and multiple) due to scratching/biting were observed on the backs of all treated animals by Day 9. Dry, flaked, abraded, and/or cracking skin was observed in all treatment groups but considered unrelated to dose level. No significant effects on body weight or food consumption were noted. No effects were noted on any hematological parameter. Mean total bilirubin levels were significantly lower in the low- and high-dose males. Mid-dose females showed increased mean albumin levels and decreased mean BUN/creatinine ratio. These effects showed no dose-related trend and were considered unrelated to treatment. No effects on organ weights were observed. The following were sporadic findings from gross pathology that were considered unrelated to treatment dilated renal pelves and dry, flaky, red, thickened, and/or scabbed skin across sexes and treated groups; dark red or small and pale ovaries in one mid and one high dose female; redness or small red foci in the lungs of one mid and one high dose male; a yellow mass and trifurcated or fused lobes in livers of two low-dose femles, one high-dose female, and one high-dose male; swollen, enlarged, reddened, and/or speckled salivary glands or nodes in one control female, one mid-dose male, and one high-dose male; an accessory spleen in a control female; a reddened/thickened area of musculature in a low-dose male; a small adrenal in gland in a mid-dose male; and a small red gastric foci in one high-dose female. Acanthosis, epidermal crusting, hyperkeratosis, and dermal inflammation was noted in both control and high-dose animals. Dermal ulceration was noted in three high-dose animals. The high-dose group showed greater incidence but slightly lower severity of inflammation compared to the controls. Other histopathological findings were considered spontaneous or naturally occurring in rats of the strain and age used in the study. The NOAEL for systemic toxicity was 50% (1.0 mL/kg in mineral oil) based on no adverse systemic effects at the highest dose tested; the test item caused mild dermal irritation.

[redacted]

2.3.2.2 [redacted]

[redacted]

Analogue for [redacted]

Test data submitted with [redacted] **-** [redacted]

- OECD 423 (Acute Oral toxicity: Acute Toxic Class Method): LD50 (female rat) > 2569 mg a.i./kg-bw
- OECD 423 (Acute Oral toxicity: Acute Toxic Class Method): LD50 (rat) > 2569 mg a.i./kg-bw; hunched posture and piloerection
- OECD 402 (Acute Dermal Toxicity): LD50 (rat) > 2000 mg/kg-bw
- OECD 402 (Acute Dermal Toxicity): LD50 (rabbit) > 2000 mg/kg-bw; chromodacryorrhoea of the snout, general erythema of the left flank, neck or treated skin and brown or yellow discoloration of the treated skin
- OECD 439 (In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method): Non-irritating in EPISKIN-SM™
- OECD 431 (In Vitro Skin Corrosion: Reconstructed Human Epidermis test method): Non-corrosive in EPI-200
- OECD 404 (Acute Dermal Irritation/Corrosion): Irritating in rabbits (very slight to well-defined erythema and very slight edema, resolved by 72 hours or 7 days). No classification required.
- OECD 439 (In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method): Non-irritating to reconstructed human epidermis in vitro
- OECD 431 (In Vitro Skin Corrosion: Reconstructed Human Epidermis test method): Non-corrosive to reconstructed human epidermis in vitro
- OECD 404 (Acute Dermal Irritation/Corrosion): Non-irritating in rabbits
- OECD 437 (Bovine Corneal Opacity and Permeability Test Method): Non-irritating in bovine corneas in vitro
- OECD 405 (Acute Eye Irritation/Corrosion): Not irritating in rabbits
- OECD 405 (Acute Eye Irritation/Corrosion): Non-irritating in rabbits
- OECD 406 (Skin Sensitization): Non-sensitizing in guinea pigs
- OECD 406 (Skin Sensitization): Non-sensitizing in guinea pigs

[redacted]

- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation
- OECD 473 (In Vitro Mammalian Chromosomal Aberration Test): Negative for induction of chromosomal aberrations in cultured human lymphocytes with and without activation
- OECD 490 (In Vitro Mammalian Cell Gene Mutation Test Using the Thymidine Kinase Gene): Negative in L5178Y mouse lymphoma cells with and without activation
- OECD 473 (In Vitro Mammalian Chromosomal Aberration Test): Non-clastogenic in cultured human lymphocytes with and without activation
- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation
- OECD 490 (In Vitro Mammalian Cell Gene Mutation Test Using the Thymidine Kinase Gene): Non-mutagenic in L5178Y mouse lymphoma cells with and without activation
- OECD 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test): Wistar(Han) rats (10/sex/group) were administered the test item (purity 44.4%) in corn oil via oral gavage at doses of 0, 100, 300, or 1000 mg/kg-bw/day. Additional non-mated animals (5/sex) were included in the control and high-dose groups for assessment of reversibility of any observed effects following a two-week recovery period. Males were dosed daily for 2 weeks prior to mating, during mating, and until one day prior to scheduled necropsy for a minimum of 28 days. Females were dosed daily for 2 weeks prior to mating, during mating, throughout gestation, for 13 to 15 days after delivery, and until one day prior to sacrifice (total of 50 to 56 days for most females). On postnatal day (PND 4), individual litters were culled to 4 pups/sex, if possible. Surviving pups were necropsied on PNDs 14 to 16. No treatment-related mortality occurred. There were no adverse treatment-related effects on clinical signs, functional observations, body weight, body weight change, food consumption, hematological parameters, clinical chemistry parameters, macroscopic or microscopic findings, reproductive parameters, or developmental parameters. An increased incidence of thyroid follicular cell hypertrophy was observed in females at 1000 mg/kg-bw/day. However, the severity grades were not increased with exposure. Furthermore, there was no treatment-related effect on thyroid weight or on serum levels thyroid hormones in females. In males, there were decreases in serum T4, but the changes did not show a clear dose-response relationship. Based on these considerations, the increased incidence of thyroid cell hypertrophy in females is not considered to be adverse; however, this finding may suggest a need for further examination. The NOAEL for systemic, reproductive, and developmental toxicity is 1000 mg/kg-bw/day.

  EPA Conclusion (reviewed with [redacted]): EPA agrees with both the reviewer and the study author. There are no consistent signs of adverse toxicity at any administered dose. Therefore, the NOAEL = 1000 mg/kg based on no adverse effects at the highest dose tested.

[redacted]

2.3.2.3 [redacted]

[redacted]

Submitted analogue for [redacted]

- OECD 423 (Acute Oral toxicity: Acute Toxic Class Method): LD50 (female rat) > 2000 mg/kg-bw
- OECD 402 (Acute Dermal Toxicity): LD50 (rat) > 2000 mg/kg-bw
- OECD 404 (Acute Dermal Irritation/Corrosion): Slightly irritating in female rabbits
- OECD 405 (Acute Eye Irritation/Corrosion): Irritating in rabbits
- OECD 406 (Skin Sensitization): Not sensitizing in guinea pigs
- OECD 474 (Mammalian Erythrocyte Micronucleus): Negative for induction of micronuclei in mice via i.p.
- OECD 473 (In Vitro Mammalian Chromosomal Aberration Test): Negative for induction of chromosomal aberrations in human peripheral blood lymphocytes with and without activation
- OECD 471 (Bacterial Reverse Mutation): Negative in Salmonella and E. coli with and without activation
- OECD Not Specified (Oral range-finding test): CrlCD (SD) rats (5/sex/group) were administered the test item via gavage at 0, 250, 500, or 1000 mg/kg-bw/day for 14 consecutive days. No mortalities were observed. One female at 500 mg/kg-bw/day exhibited opacity of the right eye and red material around the eyes during study days 12-14. This was attributed to broken and misaligned incisors during the same time, and not to the test substance. No other clinical signs were observed. No effects on body weight were observed. Statistically significant higher mean body weight gains were noted in the 1000 mg/kg-bw/day females during acclimation, and in 250 and 500 mg/kg-bw/day females from days 0-7. These differences were attributed to biological variability and not treatment since a dose-response trend was absent. No effects on food consumption were noted. No treatment-related macroscopic findings were noted at necropsy. Based on the results, the 14-day NOEL was 1000 mg/kg-bw/day and dosage levels of 250, 500, and 1000 mg/kg-bw/day were selected for a 28-day oral gavage study.
- OECD 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test): Sprague-Dawley (CrlCD(SD)) rats (12/sex/group) were administered the test item (purity 100%) in corn oil via oral gavage at doses of 0 (vehicle), 250, 500, or 1000 mg/kg-bw/day. One parental female in the

[redacted]

control group was found dead on day 35. No adverse treatment-related effects were observed on any systemic, reproductive, or developmental parameters. Significant increases in food consumption were observed at 1000 mg/kg-bw/day in males and at 500 and 1000 mg/kg-bw/day in females, but were not considered to be adverse. The NOAEL value for systemic, reproductive, and developmental toxicity was 1000 mg/kg-bw/day, based on no adverse effects at the highest dose tested.

2.3.2.4 [redacted]

No structure available

Analogue

HPVIS Database

- OECD 401: Oral LD50 (rat) > 5000 mg/kg; dark staining of the anal area
- OECD 402: Dermal LD50 (rat) > 2000 mg/kg
- OECD 474: Mammalian Erythrocyte Micronucleus Test. Negative in mice via I.p. route
- OECD 471: Bacterial reverse mutation assay. Negative in S. typhimurium strains TA98, TA100, TA1537, and TA1535 with and without metabolic activation
- OECD 407 and 421: Combined four-week repeated dose oral toxicity, reproduction and neurotoxicity screen in rats. 28-day toxicity and neurotoxicity phases: Sprague-Dawley rats (6/sex/dose, with an additional 6/sex in the control and high dose for recovery period) were administered the test substance via gavage at doses of 0, 100, 500 or 1000 mg/kg/day for the 28-day toxicity phase and 0 or 1000 mg/kg/day for the neurotoxicity phase using corn oil as a vehicle for 7 days/week for 29 or 30 days with a 2-week recovery period. There were no mortalities and no clinical signs of toxicity. Body weights and body weight change were unaffected in all treatment groups during exposure and recovery. There was a significant increase in food consumption in the 1000 mg/kg/day dose group compared to the control group during treatment and continued to be increased in females during the recovery period. Feed efficiency was lower compared to controls in 1000 mg/kg/day males at week 4 and during the first week of recovery in females; however, there was no consistent trend, and this was not considered to be toxicologically significant. There were no treatment-related effects in FOB, hematology, clinical chemistry, urinalysis, organ weights, brain size, macroscopic effects, or microscopic effects of gross lesions. Landing foot splay distance was slightly shorter in the high dose group compared to controls during treatment and recovery; however, this was similar to pretest values and was not considered toxicologically significant or treatment related. All tissues were within normal limits in the neurotoxicity study. NOELs of 1000 mg/kg/day were established for the 28-day toxicity study and neurotoxicity study based on no adverse effects at the highest dose tested.

  Reproduction phase: Sprague-Dawley rats (12/sex/dose) were administered the test substance via gavage at doses of 0, 100, 500 or 1000 mg/kg-bw/day using corn oil as a vehicle for 7 days/week for 70 day for males (29 days premating, mating, and postmating periods) and for 54-68 days for females (29 days premating through day 4 of

lactation). There were no mortalities and no clinical signs of toxicity. There were no significant effects on mean body weight, body weight change, food consumption, feed efficiency, organ weights, mating indices, mean maternal body weights during gestation, number of stillborn pups, number of pups dying after birth prior to lactation day 4, gestation index, gestation duration, mean number of live pups/litter, females completing delivery, mean number of uterine implantation scars, or corpora lutea. There was a significant increase in body weight gain over days 7-14 of gestation in the 500 and 1000 mg/kg/day dose groups; however, this was not considered treatment-related or toxicologically significant and body weights and body weight gains were comparable to controls during lactation. There were no treatment-related effects on pup body weights, pup viability indices, sex ratios, or macroscopic findings. There was a slight increase in the number of female pups in the 500 mg/kg/day dose group; however, this was not considered to be treatment-related. There were no malformations observed in stillborn or dead pups. A NOEL of 1000 mg/kg/day was established for reproductive toxicity based on no adverse effects at the highest dose tested.

ChemView Database

- OECD not specified: Dermal LD50 (rat) > 2000 mg/kg
- OECD not specified: Oral LD50 (rat) > 5000 mg/kg
- OECD not specified: Micronucleus assay. Positive in mice via I.p route
- OECD not specified: Reverse-mutation assay. Non-mutagenic in S. typhimurium strains TA98, TA100, TA1535 and TA 1537 and E. coli strain WP2uvrA
- OECD 407 and 422: Combined repeated-dose/neurotoxicity and reproductive/developmental toxicity screening test in rats via gavage. Sprague Dawley rats (12/sex/dose) were administered the test substance at doses of 0, 100, 500, or 1000 mg/kg/day in corn oil via gavage from 4 weeks prior to mating for a total of 70 days for males and until lactation day 4 in females. There were no mortalities and no clinical signs of toxicity observed. In parental animals, there were no treatment-related effects on mean body weight, weight gain, food consumption, food efficiency, organ weights, gross pathology or histopathology. There were no treatment-related effects on mating indices, number of implantation sites, corpora lutea, number of stillborn pups, number of pups dying after birth, gestation index, gestation duration, number of females completing delivery, and mean number of live pups/litter. There were no treatment-related effects on pup body weight, viability indices, sex ratio, or malformations in fetuses. NOAELs for maternal and reproductive/developmental toxicity were established at > 1000 mg/kg/day based on no adverse effects at the highest dose tested.
- OECD 407 and 422: Immunotoxicity and Neurotoxicity - Combined repeated-dose/neurotoxicity and reproductive/developmental toxicity screening test in rats via gavage. Sprague Dawley rats (6/sex/dose) were administered the test substance at doses of 0, 100, 500, or 1000 mg/kg/day in corn oil via gavage for 28 days. An additional 6/sex/dose were exposed to 0 or 1000 mg/kg/day for 28 days and then had a 2-week

[redacted]

recovery period. There were no treatment-related effects in FOB in the control and high dose groups or in the recovery groups. Landing foot splay distance was slightly shorter in the high dose group compared to controls during treatment and recovery; however, this was similar to pretest values and was not considered toxicologically significant or treatment related. There were no treatment-related effects on brain weight of histopathology. There was no evidence of neurotoxicity. No NOAEL/LOAEL reported.

- OECD 407 and 422: Combined repeated-dose/neurotoxicity and reproductive/developmental toxicity screening test in rats via gavage. Sprague Dawley rats (6/sex/dose) were administered the test substance at doses of 0, 100, 500, or 1000 mg/kg/day in corn oil via gavage for 28 days. There were no mortalities or clinical signs of toxicity. There were no treatment-related effects on body weights, body weight changes, feed efficiency, hematology, clinical chemistry, urinalysis, organ weights, brain size, or gross pathology. There was a significant increase in food consumption in the 1000 mg/kg/day dose group compared to the control group during treatment and continued to be increased in females during the recovery period. A NOAEL of > 1000 mg/kg/day was established based on no adverse effects at the highest dose tested.

Based on test substance [redacted] in ChemView Database

- OECD not specified: 28-day dermal repeat study in rats. A NOAEL of about 800 mg/kg/day was established based on no adverse effects at the highest dose tested.

2.3.2.5 [redacted]

[redacted]

Analogue

SAT Report Health Summary (from Focus Final 05-08-19): There are concerns for irritation based on test data. The use is as a dispersant, however the structure and surface tension data indicate that it is not surface active. It is not expected to cause lung effects via surfactancy or polycationic binding. The compound is a nitrogen heterocycle, however, the developmental study does not indicate this hazard at doses up to 1000 mg/kg/day. NOTE: Based on the submitted OECD 422 data that did not identify any effects at the highest tested dose, developmental effects were not considered in the risk assessment.

[redacted]

Based on the low amine content and surface tension data on the new chemical, the chemical substance is not a surfactant, thus these hazards were not considered in the risk assessment.

2.3.3 SDS Data

The SDS is not relevant to the new chemical substance (SDS appears to be for a formulated material).

2.3.4 Other Information

- From EPA chemistry report (ISIS Database, p. 2): [redacted] FGEW = [redacted] (Best case, falsely assuming that the [redacted] is entirely linear and non-cyclic and that each [redacted] is reacted with an [redacted]).
- Representative structures for low molecular weight (LMW)

[redacted]

SMILES: [redacted]

EpiSuite estimates: Log P 5.16, VP [redacted] mmHg, WS [redacted] mg/L (estimated from fragments)

[redacted]

SMILES:

[redacted]

EpiSuite estimates: Log P 9.58, VP [redacted] mmHg, WS [redacted] mg/L (estimated from fragments)

- Analogue data were submitted for analogues [redacted]

[redacted] and summarized under Section 2.3.2.

- This is a Sustainable futures case and a Sustainable Futures assessment was submitted. A document titled [redacted] was also submitted.

2.4 Exposure Routes of Interest

	Route of Interest
X	Inhalation: No systemic effects expected via inhalation based on structure and analogue data; irritation only.
X	Dermal: No systemic effects expected via the dermal route based on analogue data; irritation only.
	Ingestion: No concerns via the oral route based on analogue data.

2.5 Point of Departure (POD) Selected and Basis

No quantitative POD needed.

[redacted]

3 HUMAN HEALTH RISK

3.1 USES and EXPOSURES

3.1.1 Uses

Intended use: Lubricating additive (dispersant) for engine oils, transmission and hydraulic fluid, and gear oil applications.

3.1.2 Worker Exposure

Per Engineering Report dated 10-05-2020

3.1.2.1 Inhalation

PROC 1: [redacted] additive [redacted]
Negligible (VP < 0.001 torr); generation of respirable vapor or mist is not expected

PROC 2: [redacted] lubricant
Negligible (VP < 0.001 torr); generation of respirable vapor or mist is not expected

USE: [redacted] Lube Oil
Negligible (VP < 0.001 torr); generation of respirable vapor or mist is not expected

3.1.2.2 Dermal

PROC 1: [redacted]
[redacted]
Exposure to [redacted] at [redacted] concentration
High End PDR: [redacted] mg/day over [redacted] days/yr
LADD: [redacted] mg/kg-day over [redacted] days/yr

PROC 2: [redacted]
[redacted]
Exposure to [redacted] at [redacted] concentration
High End PDR: [redacted] mg/day over [redacted] days/yr
LADD: [redacted] mg/kg-day over [redacted] days/yr

USE: [redacted] Lube Oil
[redacted]
Exposure to [redacted] at [redacted] concentration
High End PDR: [redacted] mg/day over [redacted] days/yr
LADD: [redacted] mg/kg-day over [redacted] days/yr

3.1.3 General Population Exposure

Per Exposure Report dated 10-07-2020

3.1.3.1 Drinking Water

Not released to surface water

[redacted]

3.1.3.2 Fish Ingestion

Not released to surface water

3.1.3.3 Landfill

Exposures are expected to be negligible (below modeling thresholds)

3.1.3.4 Air/Inhalation

Stack: Exposures are expected to be negligible (below modeling thresholds)
Fugitive: No releases to fugitive air

3.1.4 Consumer Exposure

Per Exposure Report dated 10-07-2020
New chemical substance weight fraction: [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], Used Motor Oil	--	--	--	--	--	--	**2.57e+0**	**2.06e-2**	--	--

3.1.4.1 Dermal

Used Motor Oil: ADR as high as [redacted] mg/kg/day and LADD as high as [redacted] mg/kg/day

3.2 RISK CALCULATIONS

3.2.1 Worker Calculations

Irritation hazards to workers via dermal contact were identified based on the structural alert for [redacted] and test data on analogues. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards. However, exposures can be mitigated by the use of appropriate personal protective equipment (PPE), including impervious gloves and eye protection. EPA expects that employers will require and that workers will use appropriate PPE consistent with the Safety Data Sheet prepared by the submitter, in a manner adequate to protect them.

No relevant systemic hazards were identified for the new chemical substance via the dermal route; therefore, risks were not calculated. Based on no identified hazards, risks are not expected.

Risks were not evaluated for workers via inhalation exposure because exposures are expected to be negligible.

3.2.2 General Population Calculations

Risks were not evaluated because general population exposures are not expected.

[redacted]

3.2.3 Consumer Calculations

Irritation hazards to consumers via dermal contact were identified based on the structural alert for [redacted] and test data on analogues. Risks for these endpoints were not quantified due to a lack of dose-response for these hazards.

No relevant systemic hazards were identified for the new chemical substance via the dermal route; therefore, risks were not calculated. Based on no identified hazards, risks are not expected.