Health Canada Santé Canada

Evaluation Report for Category A Subcategory 1.3 Application

Application Number: 2008-4377
Application: New Active Ingredient – Maximum Residue Limits (MRL)s Only
Product: Propoxycarbazone-Sodium Technical
Registration Number: xxxxxx
Active ingredient (a.i.): Propoxycarbazone-sodium
PMRA Document Number : 1953643

Background

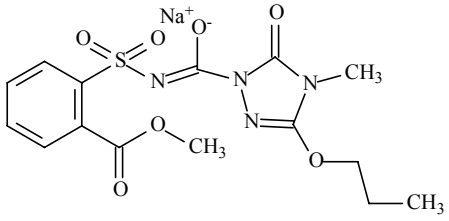
The active ingredient propoxycarbazone-sodium is registered in the United States for weed control in wheat under the trade name Olympus 70% Water Dispersible Granular Herbicide (USEPA Registration Number 264-89-AA). Propoxycarbazone-sodium has not been registered in Canada due to differing target weed spectrums between the two countries and recrop restrictions that would be necessitated following application under Canadian environmental conditions.

Purpose of Application

The purpose of this application was to establish import MRLs to cover residues of the active ingredient propoxycarbazone-sodium in/on wheat and livestock commodities.

Canada

Chemistry Assessment

Active substance	Propoxycarbazone-Sodium
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Sodium 4,5-dihydro-N-{[(methoxycarbonyl)phenyl]sulfonyl}-4-methyl-5-oxo-3-propoxy-1H-1,2,4-triazole-1-carboximidate
2. Chemical Abstracts Service (CAS)	Methyl 2-[[[(4,5-dihydro-4-methyl-5-oxo-3-propoxy-1H-1,2,4-triazol-1-yl)carbonyl]amino]sulfonyl]benzoate, sodium salt
CAS number	181274-15-7
Molecular formula	$C_{15}H_{17}N_4O_7SNa$
Molecular weight	420.4
Structural formula	
Purity of the active ingredient	95.34% (nominal concentration)

Physical and chemical properties of Propoxycarbazone-Sodium Technical

Property	Result
Colour and physical state	Colourless crystalline powder
Odour	Odourless
Melting range	230 – 240°C (decomposition)
Boiling point or range	Not applicable, the product is a solid.
Density at 20°C	1.42 g/mL
Vapour pressure at 20°C	$< 1.0 \times 10^{-8}$ Pa

Ultraviolet (UV)-visible spectrum	pH λ (nm) ε (cm^{-1} $mole^{-1}$ L) 4.0 201 4.37×10^4 7.0 204 1.90×10^4 9.0 207 1.15×10^4
Solubility in water at 20°C	42 g/L
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) Dichloromethane 1.5 *n*-Heptane <0.1 Xylene <0.1 Isopropanol <0.1
n-Octanol-water partition coefficient (K_{ow})	pH log Kow 7.0 -1.55 4.0 -0.30 9.0 -1.59
Dissociation constant (pK_a)	The free acid produced by protonation under acidic conditions has a pKa value of 2.1.
Stability (temperature, metal)	The product is thermally stable at ambient temperature under air

Physical and chemical properties of Olympus 70% Water Dispersible Granular Herbicide

Property	Result
Colour	Waived (USEPA Pesticide Regulation Notice PR 92-5)
Odour	Waived (USEPA Pesticide Regulation Notice PR 92-5)
Physical state	Solid
Formulation type	Granular
Guarantee	70% (nominal concentration)
Container material and description	Not provided
Density	0.45 g/cm^3
pH of 10% dispersion in water at 25°C	7.6
Oxidizing or reducing action	The product does not contain any ingredient (technical or inert) which is considered to be an oxidizing or reducing agent.

Storage stability	Not required, it is an import MRL Relative A.I. loss, compared to the test standard, was 0.0 - 0.97% during a 2 week test period at 50°C (based on corrosion evaluation).
Corrosion characteristics	Not expected to be corrosive to storage container. Relative A.I. loss, compared to the test standard, was 0.0 - 0.97 % during 2 week test period at 50°C.
Explodability	No impact explosive characteristics are expected on the basis of the chemical nature of the formulation ingredients.

The methods provided for the analysis of the active ingredient and the impurities in Propoxycarbazone-Sodium Technical have been validated and assessed to be acceptable for the determinations. The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

Health Assessment

Toxicology summary

The PMRA conducted a detailed review of the toxicological database for propoxycarbazone-sodium. The database consists of an array of laboratory animal (*in vivo*) and cell culture (*in vitro*) toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is acceptable, and the database is considered adequate to characterize the toxicity of propoxycarbazone-sodium.

Laboratory studies in the rat demonstrated that the absorption of radiolabelled propoxycarbazone-sodium was rapid but incomplete following oral administration. Peak plasma concentrations were seen about 1 h after exposure. About 21-31% of the administered dose (AD) was absorbed and eventually excreted in the urine within 48 h. The majority of the AD (64-83%) was excreted mostly unchanged in the feces within 48 h. Negligible propoxycarbazone residues were detected in expired air. Tissue distribution of propoxycarbazone residues was limited to the gastrointestinal (GI) tract, liver, and kidneys at low concentrations. The total propoxycarbazone residue remaining in tissues was low and there was no evidence of bioaccumulation for all dose levels tested. Metabolism of propoxycarbazone-sodium in the rat was limited. Analysis of the metabolites indicated that only a small number of minor metabolites, each accounting for less than 3% of the AD, were detected in the urine and feces, with the exception of a fecal metabolite which accounted for 2-9% of the AD. There were no notable gender differences in the metabolic profile of propoxycarbazone-sodium in the rat.

Propoxycarbazone-sodium and its metabolites and impurities are of low acute toxicity by the oral route in rats. Short-term toxicity studies in laboratory animals (mouse, rat, dog) demonstrated that propoxycarbazone-sodium induced systemic toxicity only at very high dose levels. The effects invariably included lower food consumption and body-weight gains, increased water intake, and, in the rat only, irritation of the forestomach. Gross and histopathology changes in other tissues were not evident.

In vivo/*in vitro* genotoxicity studies of propoxycarbazone-sodium assessing gene mutation, chromosome aberration, and unscheduled DNA synthesis showed negative genotoxic findings. Metabolites and impurities of propoxycarbazone-sodium were not mutagenic when tested *in vitro* microbial mutation assays.

Long-term studies of propoxycarbazone-sodium in mice and rats showed toxic effects similar to those observed in shorter-term studies. Sufficiently high dose levels were tested in these rodent species and there was no evidence of oncogenic potential.

A reproductive toxicity study in rats demonstrated slight changes in the estrous cycle at a high dose that also induced maternal toxicity (decreased food efficiency, epithelial vacuolation of forestomach). However, there was no evidence of offspring toxicity. Developmental toxicity studies in the rat and rabbit did not demonstrate any evidence of teratogenicity. In rats tested at the limit dose, there was no evidence of maternal or developmental toxicity. In the rabbit, oral exposure of propoxycarbazone-sodium resulted in maternal toxicity (decreased food and water intake, body-weight gain, and GI tract effects) and abortions. Growth and development of the fetuses were delayed at the maternally toxic doses.

Acute and short-term neurotoxicity data are not required for the registration of propoxycarbazone-sodium to establish the Maximum Residue Limits (MRLs) in Canada. However, these neurotoxicity data on propoxycarbazone-sodium are available. Evaluation of these data by the USEPA indicated that propoxycarbazone-sodium was not neurotoxic and there were no triggers for the requirement of a developmental neurotoxicity study.

The results of the acute and chronic tests conducted on laboratory animals with propoxycarbazone-sodium, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Tables 1, 2, and 3 of Appendix I.

Incident reports

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the PMRA website. Incidents from Canada and the United States were searched and reviewed for propoxycarbazone-sodium.

As of July 16, 2010, no incidents involving adverse effects resulting from exposure to propoxycarbazone have been reported to PMRA.

In the USA, propoxycarbazone-sodium has been registered for use on wheat since 2004. A search of the US databases including the Office of Pesticides Program Incident Data System

(IDS), Poison Control Center, California Department of Pesticide Regulation (CDPR), and the National Institute of Occupational Safety and Health's Sentinel Event Notification System for Occupational Risks (NIOSH SENSOR) was conducted and did not identify any human incident involving propoxycarbazone-sodium.

As there were no incidents reported, the evaluation and conclusions of the current toxicity database and human health risk assessment were not affected.

PCPA hazard characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* (PCPA) requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, adequate data are available for propoxycarbazone-sodium, including developmental toxicity studies in rats and rabbits and reproductive toxicity studies in rats.

With respect to identified concerns relevant to the assessment of risk to infants and children, no evidence of increased susceptibility was seen following in utero exposure to rats or rabbits in the developmental toxicity studies. In the rat developmental toxicity study, there were no maternal or developmental effects at the limit dose. In the rabbit developmental toxicity study, the abortions seen at high doses occurred late in gestation and were associated with maternal toxicity (decreased food and water consumption, body-weight gain, and GI tract pathology). In the rat reproductive toxicity study, adverse offspring effects were not identified. Based on these data, there is a low level of concern for pre- or post-natal toxicity associated with propoxycarbazone-sodium exposure. In light of these findings and the completeness of the database, the PCPA factor was reduced from 10-fold to 1-fold.

Human risk assessment

There were no effects in the database warranting the establishment of an acute reference dose.

To estimate dietary risk from long-term repeat exposure, the reproductive toxicity study in the rat is considered relevant for the establishment of the ADI. Systemic toxicity in the parents was demonstrated at the LOAEL of 297 mg/kg bw/d based on epithelial vacuolation in the forestomach. The NOAEL for parental toxicity was 75 mg/kg bw/d. For ADI determination, the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. For the reasons outlined in the PCPA Hazard Characterization section, the PCPA factor was reduced to 1-fold. The composite assessment factor (CAF) is therefore 100. This ADI is considered to be protective of all sub-populations including women of child-bearing age and nursing infants.

The ADI, calculated according to the following formula, is 0.75 mg/kg bw/d:

$$ADI = \frac{NOAEL}{CAF} = \frac{75 \text{ mg/kg bw/d}}{100} = 0.75 \text{ mg/kg bw/d}$$

No toxicological end-points are proposed for occupational risk assessment because products containing propoxycarbazone-sodium are not to be used in Canada.

Food residue exposure assessment

The nature of propoxycarbazone-sodium in wheat is adequately understood based on the submitted wheat metabolism studies. The general metabolic pathway in wheat involves hydroxylation of the propoxy side chain of propoxycarbazone to give Pr-2-OH MKH 6561. Hydrolysis of Pr-2-OH MKH 6561 then gave Pr-2-OH NMT and, probably, the sulfonamide methyl ester, which was not observed in any of the wheat matrices. Hydrolysis of the sulfonamide methyl ester gave sulfonamide acid, which was in equilibrium with saccharin. A minor metabolic pathway was demethylation of propoxycarbazone to yield N-desmethyl MKH 6561.

A summary of the residue definition for propoxycarbazone is provided in the following table.

Matrix	Dietary Risk Assessment	Enforcement Assessment
Wheat	Propoxycarbazone, and the metabolite Pr-2-OH MKH 6561	Propoxycarbazone, and the metabolite Pr-2-OH MKH 6561

An LC-MS/MS (liquid chromatography with tandem mass spectrometry) method was developed and proposed for data gathering and enforcement purposes in wheat and livestock commodities. This method fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. Acceptable recoveries (70–120%) were obtained in wheat matrices. The proposed enforcement method was successfully validated by an independent laboratory using wheat grain and beef liver samples. Adequate extraction efficiencies were demonstrated using radiolabelled wheat and livestock samples.

Residues of propoxycarbazone and the metabolite Pr-2-OH MKH 6561 were stable at <-18°C for up to 540 days (~18 months) in wheat green material, grain and straw.

A total of 21 trials were conducted in/on wheat (one trail in each of Zones 2, 4, 6 and 11; 6 trials in each of Zones 5 and 8; 5 trials in Zone 7) during the 1996 to 1997 growing season. Additional wheat forage samples were generated from a second study during the 2003 to 2004 growing season (20 trials: one trial in each of Zones 2, 4, 6 and 11; 6 trials in Zone 8; 5 trials in each of Zones 5 and 7). For both studies, foliar applications were made to wheat (spring and winter wheat) using a wettable granular formulation containing 70% propoxycarbazone-sodium (70 WG). Data from these field trials are summarized in Appendix I, Table 4.

As residues of propoxycarbazone were all < LOQ (<0.02 ppm) in wheat grain when treated at exaggerated rates, processing data were not required.

Based on the residue data provided, an MRL of 0.02 ppm will be recommended as shown in the following table.

Commodity	Recommended MRL (ppm)
Wheat	0.02

Chronic dietary risk assessments, using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.16), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998, coupled with MRL-level residues that were used for all imported crops and livestock commodities, was conducted. It is demonstrated that chronic dietary exposure from all propoxycarbazone food uses for the general population is 0.1% of the acceptable daily intake (ADI). The highest exposure and risk estimate is for children 1 to 2 and 3 to 5 years old at 0.2% of the ADI (0.001460 mg/kg bw/day) (Table 4).

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore, no acute dietary exposure assessment was conducted.

Environmental Assessment

An environmental assessment was not required for this application.

Value Assessment

A value assessment was not required for this application.

Conclusions

Following the review of all available data, an MRL of 0.02 ppm for propoxycarbazone-sodium in/on imported wheat is proposed. Total residues of propoxycarbazone and the metabolite Pr-2-OH MKH 6561 will not pose an unacceptable risk to any segment of the population, including infants, children, adults and seniors.

References

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Appendix I Tables

Table 1 Acute Oral Toxicity of Propoxycarbazone-Sodium (MKH 6561) and Metabolites/Impurities

Species, strain (test compound)	Results	Comments	Reference
Rat, Wistar (MKH 6561)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654546
Rat, Wistar (bissulfonylurea-MKH 6561)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654548
Rat, Wistar (KTS 9061)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654550

Species, strain (test compound)	Results	Comments	Reference
Rat, Wistar (MKH 8394)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654553
Rat, Wistar (4-OH-saccharine)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654555
Rat, Wistar (methylthio analogue free acid – MKH 6561)	LD_{50} ♂♀ > 5000 mg/kg bw	Low toxicity	1654558

Table 2 Short- and Long-term Toxicity Profile of Propoxycarbazone-Sodium

Study type	Species, strain / test compound / dose levels	Results and comments	Reference
Short-term toxicity - propoxycarbazone			
28-Day dietary	Rat, Wistar / KTS 9061 (metabolite in rat, wheat, rotational crop) 0, 800, 4000, 10000 ppm ♂: 0, 74, 363, 905; ♀: 0, 71, 354, 880 mg/kg bw/d	No NOAEL set for range-finding study	1654589
5-Week dietary	Mouse, $B6C3F_1$ / MKH 6561 0, 100, 1000, 10000 ppm ♂: 0, 42, 394, 5579; ♀: 0, 64, 547, 5989 mg/kg bw/d	No NOAEL set for range-finding study	1654560
28-Day dietary	Rat, Wistar / MKH 6561 0, 800, 4000, 10000, 20000 ppm ♂: 0, 80, 392, 1074, 2146; ♀: 0, 79, 399, 985, 2305 mg/kg bw/d	No NOAEL set for range-finding study	1654563
64-Day dietary	Dog, beagle / MKH 6561 0, 1000, 5000, 10000, 40000 ppm ♂ = 0, 28, 140, 322, 1407; ♀ = 0, 32, 134, 286, 1181 mg/kg bw/d	No NOAEL set for range-finding study	1654595
14-Week dietary	Mouse, $B6C3F_1$ / MKH 6561 0, 625, 2500, 10000 ppm ♂: 0, 205, 860, 3926; ♀: 0, 307, 1159, 5109 mg/kg bw/d	NOAEL: ♂ = 625 ppm or 205 mg/kg bw/d ♀ = 2500 ppm or 1159 mg/kg bw/d (↓ bw)	1654579
14-Week dietary with 4-week recovery	Rat, Wistar / MKH 6561 0, 0 (recovery), 250, 1000, 4000, 20000, 20000 (recovery) ppm ♂ = 0, 17.4, 73, 286, 1508; ♀ = 0, 21.6, 82, 351, 1770 mg/kg bw/d	NOAEL = 4000 ppm ♂= 286, ♀ = 351 mg/kg bw/d LOAEL: 20000 ppm ♂ = 1508, ♀ = 1770 mg/kg bw/d based on forestomach irritation	1654568

Study type	Species, strain / test compound / dose levels	Results and comments	Reference
1-Year dietary	Dog, beagle / MKH 6561 0, 2000, 10000, 25000 ppm ♂ = 0, 52, 258, 631; ♀ = 0, 56, 236, 605 mg/kg bw/d	NOAEL: 10000 ppm ♂ = 258, ♀ = 236 mg/kg bw/d LOAEL: 25000 ppm ♂ = 631, ♀ = 605 mg/kg bw/d based on ↓ food efficiency	1654604
Chronic toxicity and oncogenicity			
107-Week dietary oncogenicity	Mouse, B6C3F$_1$ MKH 6561; 0, 280, 1400, 7000 ppm ♂ = 0, 75, 369, 1881; ♀ = 0, 126, 627, 3106 mg/kg bw/d	NOAEL = 1400 ppm ♂ = 369; ♀ = 627 mg/kg bw/d LOAEL = 7000 ppm ♂ = 1881; ♀ =3106 mg/kg bw/d based on ↓ bw & bwg No evidence of oncogenicity	1654621
2-Year dietary/ oncogenicity	Rat, Fischer 344 / MKH 6561 0, 1000, 10000, 20000 ppm ♂ = 0, 43, 459, 924; ♀ = 0, 49, 525, 1049 mg/kg bw/d	NOAEL = 1000 ppm ♂ = 34; ♀ = 49 mg/kg bw/d LOAEL = 10000 ppm ♂ = 459; ♀ = 525 mg/kg bw/d based on ↓ bwg No evidence of oncogenicity	1654648
Reproduction and developmental toxicity			
1-Generation reproductive toxicity	Rat, Wistar / MKH 6561 0, 1000, 5000, 20000 ppm ♂: 0, 61, 230, 1230 ♀: 0, 69, 384, 1542 mg/kg bw/d (premating intake)	No NOAELs set because this is a range-finding study	1654751

Study type	Species, strain / test compound / dose levels	Results and comments	Reference
2-Generation reproductive toxicity	Rat, Wistar / MKH 6561 0, 1000, 4000, 16000 ppm ♂ = F_0: 0, 75, 297, 1231 F_1: 0, 80, 323, 1314 ♀ = F_0: 0, 93, 374, 1605 F_1: 0, 104, 414, 1908 mg/kg bw/d (premating intake)	NOAELs: Parental systemic toxicity: ♂ = 1000 ppm or 75 mg/kg bw/d; ♀ = 4000 ppm or 374 mg/kg bw/d Offspring toxicity = 16000 ppm; ♂ = 1231, ♀ = 1605 mg/kg bw/d Reproductive toxicity: ♂ = 16000 ppm, or 1231 mg/kg bw/d; ♀ = 4000 ppm or 374 mg/kg bw/d LOAELs: Parental systemic toxicity: ♂ = 4000 ppm or 297 mg/kg bw/d based on microscopic lesions in forestomach; ♀ = 16000 ppm or 1605 mg/kg bw/d based on ↓ food efficiency Offspring toxicity = not established Reproductive toxicity = ♂ = not established ♀ = 16000 ppm or 1605 mg/kg bw/d based on changes in oestrous cycle	1654755
Developmental toxicity	Rat, Wistar / MKH 6561 0, 100, 300, 1000 mg/kg bw/d	NOAELs: Maternal and developmental toxicity = 1000 mg/kg bw/d (HDT) LOAELs: not established No evidence of teratogenicity	1654774
	Rabbit, Himalayan / MKH 6561 0, 20, 100, 500, 1000 mg/kg bw/d	NOAELs: mg/kg bw/d Maternal and developmental toxicity = 500 LOAELs: mg/kg bw/d Maternal = 500 (based on ↑ abortion, ↓ bw and GI tract effects) Developmental = 500 (based on ↑ abortion; ↓ fetal bw) No evidence of teratogenicity	1654787
Neurotoxicity			

Study type	Species, strain / test compound / dose levels	Results and comments	Reference
Acute	Rat, Wistar / MKH 6561 0, 200, 800, 2000 mg/kg bw	LOAEL: ♂ = not established ; ♀ =2000 mg/kg bw (based on ↓ bwg) NOAEL: Systemic ♂ = 2000, ♀ = 800 mg/kg bw Neurotoxicity ♂♀ = 2000 mg/kg bw	1654536 (reviewed by USEPA)
90-Day	Rat, Wistar / MKH 6561 0, 1000, 4000, 20000 ppm ♂ = 0, 64, 252, 1321 ♀ = 0, 79, 312, 1651 mg/kg bw/d	LOAEL: Systemic ♂♀ = not established NOAEL: Systemic and neurotoxicity ♂♀ = 20000 ppm ♂ = 1321 mg/kg bw/d ♀ = 1651 mg/kg bw/d	
Developmental		No trigger for developmental neurotoxicity data	
Metabolism/toxicokinetics			
Metabolism	Rat, Wistar / MKH 6561	Absorption: rapid but incomplete (~21-31%); plasma peak concentrations at 1 h post-dosing; T_{max} = 0.33 - 0.81 h Distribution: rapid, biphasic (~1 and 11 h post-dosing), mainly in gut, liver, and kidneys; but the level declined rapidly; no evidence of bioaccumulation. ♀ = Excretion: rapid; mainly in feces (64-83%); urinary elimination secondary (~21-31%); negligible via expired air (<0.15%). Metabolism: minimal; unchanged parent compound the main compound excreted.	1654848 1654836 1654857
Genotoxicity			
Gene mutations in bacteria *in*	*Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 / MKH 6561	negative	1654801

Study type	Species, strain / test compound / dose levels	Results and comments	Reference
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / KTS9061, a metabolite	negative	1654804
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / Methylthio analogue free acid - MKH 6561	negative	1654807
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / KTS 9304	negative	1654810
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / MKH 8394	negative	1654813
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / 4-OH-saccharine	negative	1654815
	Salmonella typhimurium strains TA98, TA100, TA102, TA1535, TA1537 / bissulfonylurea - MKH 6561, a byproduct of MKH6561	negative	1654815
Gene mutations in mammalian cells *in vitro*	Chinese hamster V79 cells (HGPRT locus) / MKH 6561	negative	1654826
Chromosome aberrations *in vitro*	Chinese hamster V79 cells / MKH 6561	negative	1654821
	Chinese hamster V79 cells / KTS 9061	negative	1654828
In vitro unscheduled DNA synthesis	Primary rat hepatocyte cultures / MKH 6561	negative	1654824
In vivo mouse micronucleus assay	mouse, CD-1 / MKH 6561; ip injection of 2500 mg/kg bw	negative	1654828

Table 3 Toxicology Endpoints for Use in Health Risk Assessment for Propoxycarbazone-Sodium

Exposure scenario	NOAEL, mg/kg bw/d	Study	Endpoint	CAF[1]	ARfD / ADI
Acute dietary (ARfD), all population	Not required because of low acute toxicity				
Chronic dietary (ADI), all population	75	Rat reproductive toxicity	Stomach irritation	100	0.75 mg/kg bw/d

[1] CAF (Composite Assessment Factor) refers to the total uncertainty and PCPA factors for dietary risk assessment.

Table 4 Summary of Propoxycarbazone Residues Data from Crop Field Trials

Commodity	Total Rate (g a.i./ha)	PHI[1] (days)	Total Propoxycarbazone Residue Levels (ppm)						
			n	Min.	Max.	HAFT$_2$	Median	Mean	Std. Dev.
Wheat Forage	45	0-56	104	<0.02	11	11	0.3	1.7	0.24
	60	0-60	53	<0.02	2.8	2.7	0.5	0.76	0.11
Wheat Hay	45	38-88	53	<0.02	<0.06	<0.06	<0.02	0.024	0.001
	60	15-88	38	<0.02	<0.12	<0.12	<0.02	<0.03	0.004
Wheat Straw	45	72-124	42	<0.02	<0.02	<0.02	<0.02	<0.02	0
	60	81-124	32	<0.02	<0.03	<0.03	<0.02	<0.021	0.0004
Wheat Grain	45	71-124	42	<0.02	<0.02	<0.02	<0.02	<0.02	0
	60	81-124	32	<0.02	<0.02	<0.02	<0.02	<0.02	0

Table 5 Summary of Dietary Exposure and Risk from Food Only

Basic chronic non-cancer dietary risk	Population	Estimated risk % of Acceptable Daily Intake (ADI)

		Food Only	Food and Water*
	All infants < 1 year	0.1	-
	Children 1–2 years	0.2	-
	Children 3 to 5 years	0.2	-
	Children 6–12 years	0.1	-
	Youth 13–19 years	0.0	-
	Adults 20–49 years	0.0	-
	Adults 50+ years	0.0	-
	Females 13 to 49 yrs	0.0	-
	Total population	0.1	-

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