

5.18 IMAZAMOX (276)

TOXICOLOGY

Imazamox (BAS 720 H) is the ISO-approved common name for (+)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-5-(methoxymethyl) nicotinic acid (IUPAC) (CAS No. 114311-32-9). Imazamox is an imidazolinone herbicide used pre- or post-emergence of weeds.

Imazamox has not been evaluated previously by JMPR and was reviewed by the present Meeting at the request of CCPR.

All critical studies contained statements of compliance with GLP, unless otherwise specified.

Biochemical aspects

In rats, imazamox was rapidly absorbed, and the oral absorption was approximately 75% of the administered dose. Urine was the major route of excretion (> 74%). Most of the elimination occurred within the first 24 hours after dosing, as unchanged parent compound. Smaller amounts of the test substance were excreted through faeces (> 19%). Only trace amounts of tissue residue were detected. Imazamox appears not to be metabolized. Trace levels of imazamox-related compounds detected in the urine and faeces were attributed to the presence of impurities in the dosing solution, not to rat metabolism.

A comparative in vitro metabolism study was performed in liver microsomes from mice, rats, rabbits, dogs and humans. Under the conditions of the study, no metabolites of imazamox were detected.

Toxicological data

Imazamox was of low toxicity after oral, dermal and inhalation exposure. The oral LD₅₀ in rats was greater than 5000 mg/kg bw. The dermal LD₅₀ in rats was greater than 4000 mg/kg bw, and the inhalation LC₅₀ in rats was greater than 1.6 mg/L. Imazamox was neither a skin irritant nor an eye irritant in rabbits. In a guinea-pig maximization test, no skin sensitization occurred.

In short-term toxicity studies in rats with dietary administration of imazamox over 28 and 90 days, no adverse effects were reported up to the top dose levels, which were at least 1500 mg/kg bw per day. Similarly, in 90-day and 1-year studies, no adverse effects were reported in dogs receiving imazamox in the diet up to the top dose levels, which were at least 1100 mg/kg bw per day. In long-term toxicity and carcinogenicity studies in mice and rats, no signs of systemic toxicity or treatment-related increases in neoplastic lesions were reported up to the highest dose levels tested, which were approximately 1000 mg/kg bw per day.

The Meeting concluded that imazamox is not carcinogenic in mice or rats.

Imazamox was tested for genotoxicity in an adequate range of assays, both in vitro and in vivo. No evidence of genotoxicity was found.

The Meeting concluded that imazamox is unlikely to be genotoxic.

In view of the lack of genotoxicity and the absence of carcinogenicity in mice and rats, the Meeting concluded that imazamox is unlikely to pose a carcinogenic risk to humans.

In a two-generation study in rats, there was no evidence of adverse effects on parental animals, offspring or reproduction up to the highest tested dietary imazamox concentration of 20 000 ppm (equal to 1554 mg/kg bw per day).

In a rat developmental toxicity study that tested imazamox doses of 0, 100, 500 and 1000 mg/kg bw per day, the NOAEL for maternal toxicity was 500 mg/kg bw per day, for reduced

body weight gain and feed consumption at 1000 mg/kg bw per day. The NOAEL for embryo and fetal toxicity was 1000 mg/kg bw per day, the highest dose tested.

In a rabbit developmental toxicity study that tested imazamox doses of 0, 300, 600 and 900 mg/kg bw per day, the NOAEL for maternal toxicity was 300 mg/kg bw per day, for decreased feed intake during the dosing period at 600 mg/kg bw per day, which was of equivocal toxicological relevance. Effects on feed intake were not observed during the first days of dosing. The NOAEL for embryo and fetal toxicity was 300 mg/kg bw per day, based on an increased incidence of both absent intermediate lung lobes and hemivertebrae at 600 mg/kg bw per day.

The Meeting concluded that imazamox is teratogenic in rabbits, but not in rats.

Toxicological data on metabolites and/or degradates

The oral LD₅₀s of metabolites CL 312622 (2-(4-isopropyl-4-methyl-5-oxo-3*H*-imidazol-2-yl)pyridine-3,5-dicarboxylic acid) and CL 263284 (5-(hydroxymethyl)-2-(4-isopropyl-4-methyl-5-oxo-3*H*-imidazol-2-yl)pyridine-3-carboxylic acid) were greater than 5000 mg/kg bw in rats and mice, respectively. CL 312622 was tested for genotoxicity in an adequate range of assays in vitro. No evidence of genotoxicity was observed. CL 263284 was tested for genotoxicity in an adequate range of assays in vitro and in vivo. It gave a positive response in the in vitro micronucleus assay, but was negative in the in vivo micronucleus assay. In a 28-day repeated-dose toxicity study in rats with CL 263284, which tested dietary concentrations of 0, 1200, 4000 and 12 000 ppm (equal to 0, 102, 333 and 1004 mg/kg bw per day for males and 0, 104, 339 and 1028 mg/kg bw per day for females, respectively), the NOAEL was 4000 ppm (equal to 333 mg/kg bw per day), based on lower body weights and significantly lower body weight gains observed in males treated with 12 000 ppm. No effects were observed in females up to the highest tested dietary concentration of 12 000 ppm (equal to 1028 mg/kg bw per day). CL 189215 (2-(4-isopropyl-4-methyl-5-oxo-3*H*-imidazol-2-yl)-5-({[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}methyl)pyridine-3-carboxylic acid) was tested for genotoxicity in a range of assays in vitro, and there was no evidence of genotoxicity.

Human data

No information was provided on the health of workers involved in the manufacture or use of imazamox. No information on accidental or intentional poisoning in humans is available.

The Meeting concluded that the existing database on imazamox was adequate to characterize the potential hazards to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–3 mg/kg bw based on the NOAEL of 300 mg/kg bw per day for reduced feed intake in dams of equivocal toxicological relevance and an increased incidence of both absent intermediate lung lobes and hemivertebrae in the developmental toxicity study in rabbits, using a safety factor of 100.

The Meeting established an ARfD of 3 mg/kg bw based on the NOAEL of 300 mg/kg bw per day for an increased incidence of both absent intermediate lung lobes and hemivertebrae in the developmental toxicity study in rabbits, using a safety factor of 100. Considering the uncertainty as to whether the observed effects on prenatal bone development are also relevant for children's bone growth (bone remodelling), the ARfD is applicable to the whole population.

The plant metabolite CL 263284 is an *O*-demethylation product of imazamox and is a common metabolite with imazapic. Although there is some indication of slightly higher toxicity of this metabolite when compared with imazamox in a 28-day toxicity study in rats, the effects observed were mild changes in body weight gain in males only. Taking into account the close structural similarity to imazamox and the effects and effect levels observed in the developmental toxicity study

in rats with imazamox, the Meeting concluded that CL 263284 is of similar toxicity to imazamox and would be covered by the ADI and ARfD for imazamox.

A toxicological monograph was prepared.

Levels relevant to risk assessment of imazamox

Species	Study	Effect	NOAEL	LOAEL
Mouse	Eighteen-month study of carcinogenicity ^a	Toxicity	7 000 ppm, equal to 1 053 mg/kg bw per day ^b	–
		Carcinogenicity	7 000 ppm, equal to 1 053 mg/kg bw per day ^b	–
Rat	Ninety-day study of toxicity ^a	Toxicity	20 000 ppm, equal to 1 550 mg/kg bw per day ^b	–
	Two-year study of toxicity and carcinogenicity ^a	Toxicity	20 000 ppm, equal to 1 068 mg/kg bw per day ^b	–
		Carcinogenicity	20 000 ppm, equal to 1 068 mg/kg bw per day ^b	–
	Two-generation reproductive toxicity study ^a	Parental toxicity	20 000 ppm, equal to 1 554 mg/kg bw per day ^b	–
		Reproductive toxicity	20 000 ppm, equal to 1 554 mg/kg bw per day ^b	–
		Offspring toxicity	20 000 ppm, equal to 1 554 mg/kg bw per day ^b	–
Developmental toxicity study ^c	Maternal toxicity	500 mg/kg bw per day	1 000 mg/kg bw per day	
	Embryo and fetal toxicity	1 000 mg/kg bw per day ^b	–	
Rabbit	Developmental toxicity study ^c	Maternal toxicity	300 mg/kg bw per day	600 mg/kg bw per day
		Embryo and fetal toxicity	300 mg/kg bw per day	600 mg/kg bw per day
Dog	Ninety-day and 1-year studies of toxicity ^{a,d}	Toxicity	40 000 ppm, equal to 1 333 mg/kg bw per day ^b	–

^a Dietary administration.

^b Highest dose tested.

^c Gavage administration.

^d Two or more studies combined.

Estimate of acceptable daily intake (ADI)

0–3 mg/kg bw

Estimate of acute reference dose (ARfD)

3 mg/kg bw

Information that would be useful for the continued evaluation of the compound

Results from epidemiological, occupational health and other such observational studies of human exposures

Critical end-points for setting guidance values for exposure to imazamox

<i>Absorption, distribution, excretion and metabolism in mammals</i>	
Rate and extent of oral absorption	Rats: T _{max} = 0.5–1 hour; extensive, ~75%
Dermal absorption	No data
Distribution	Widespread tissue distribution
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	Excretion mainly via urine within 48 hours
Metabolism in animals	No metabolism
Toxicologically significant compounds in animals and plants	Parent compound
<i>Acute toxicity</i>	
Rat, LD ₅₀ , oral	> 5 000 mg/kg bw
Rat, LD ₅₀ , dermal	> 4 000 mg/kg bw
Rat, LC ₅₀ , inhalation	> 1.6 mg/L
Rabbit, dermal irritation	Not irritating
Rabbit, ocular irritation	Not irritating
Guinea-pig, dermal sensitization	Not sensitizing (maximization test)
<i>Short-term studies of toxicity</i>	
Target/critical effect	No adverse effects
Lowest relevant oral NOAEL	> 1 000 mg/kg bw per day, highest dose tested (rat and dog)
Lowest relevant dermal NOAEL	> 1 000 mg/kg bw per day, highest dose tested (rat)
Lowest relevant inhalation NOAEC	No data
<i>Long-term studies of toxicity and carcinogenicity</i>	
Target/critical effect	No adverse effects
Lowest relevant NOAEL	> ~1000 mg/kg bw per day, highest dose tested (rat and mouse)
Carcinogenicity	Unlikely to pose a carcinogenic risk to humans
<i>Genotoxicity</i>	
	Unlikely to be genotoxic
<i>Reproductive toxicity</i>	
Target/critical effect	No evidence of reproductive toxicity (rat)
Lowest relevant parental NOAEL	1 554 mg/kg bw per day, highest dose tested
Lowest relevant offspring NOAEL	1 554 mg/kg bw per day, highest dose tested
Lowest relevant reproductive NOAEL	1 554 mg/kg bw per day, highest dose tested
<i>Developmental toxicity</i>	
Target/critical effect	Increased incidence of both absent intermediate lung lobes and hemivertebrae at maternally toxic doses (rabbits)
Lowest relevant maternal NOAEL	300 mg/kg bw per day (rabbit)
Lowest relevant embryo/fetal NOAEL	300 mg/kg bw per day (rabbit)

<i>Neurotoxicity</i>	
Acute neurotoxicity NOAEL	No data
Subchronic neurotoxicity NOAEL	No data
Developmental neurotoxicity NOAEL	No data
<i>Toxicological studies on CL 312622 (plant metabolite)</i>	
Rat LD ₅₀ , oral	> 5 000 mg/kg bw
Genotoxicity	Unlikely to be genotoxic
<i>Toxicological studies on CL 263284 (plant metabolite)</i>	
Mouse LD ₅₀ , oral	> 5 000 mg/kg bw
Genotoxicity	Unlikely to be genotoxic in vivo
Twenty-eight day, rat	NOAEL: 333 mg/kg bw per day (based on reduced body weight and body weight gain in males)
<i>Toxicological studies on CL 189215 (plant metabolite)</i>	
Genotoxicity	Unlikely to be genotoxic
<i>Medical data</i>	
	No data

Summary

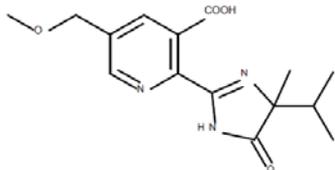
	Value	Study	Safety factor
ADI	0–3 mg/kg bw	Developmental toxicity study (rabbit)	100
ARfD	3 mg/kg bw	Developmental toxicity study (rabbit)	100

RESIDUE AND ANALYTICAL ASPECTS

Imazamox is an imidazolinone herbicide registered in many countries to control a wide spectrum of grass and broadleaf weeds. At the Forty-fourth Session of the CCPR (2012)¹, it was scheduled for evaluation as a new compound by the 2014 JMPR.

The Meeting received information on the physical and chemical properties, animal and plant metabolism, environmental fate, analytical methods, storage stability, use patterns, supervised trials and processing studies.

The following abbreviated names were used for the metabolites discussed below.

Code (MW)	IUPAC chemical name	Structure
CL 299263 (305) Imazamox; BAS 720 H	(<i>RS</i>)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)-5-methoxymethylnicotinic acid	

¹ REP12/PR-Appendix XIII

Code (MW)	IUPAC chemical name	Structure
CL 263284 (291) M715H001	5-(hydroxymethyl)-2-(4-isopropyl-4-methyl-5-oxo-2-imidazol-2-yl) nicotinic acid	
CL 189215 (453.5) M715H002	5-[(β-glucopyranosyl oxy) methyl]-2-(4-isopropyl-4-methyl-5-oxo-2-imidazol-2-yl) nicotinic acid	
CL 312622 (305) M720H002	2-(4-isopropyl-4-methyl-5-oxo-2-imidazol-2-yl)-3,5-pyridine-dicarboxylic acid	
CL 354825 (277)	5-hydroxy-6-(4-isopropyl-4-methyl-5-oxo-2-imidazol-2-yl)-nicotinic acid	
CL 336554 (323)	2-[(1-carbamoyl-1,2-dimethylpropyl) carbamoyl]-5-(methoxymethyl)-nicotinic acid	
CL 152795	2-[(1-carbamoyl-1,2-dimethylpropyl) carbamoyl]-3,5-pyridinedicarboxylic acid	

Animal metabolism

The Meeting received metabolism studies on imazamox, CL 263284 (hydroxymethyl) and CL 312622 (dicarboxylic acid) orally administered to lactating goats and laying hens.

Imazamox

Lactating goats were orally administered single daily doses of [pyridine-6-¹⁴C]-imazamox, via gelatin capsules, for seven consecutive days at either 2.1 or 12 ppm. Kidney, liver, leg and loin muscle, and omental fat samples were collected approximately 20 hours after the last dosing.

In the goat the imazamox was mainly excreted in urine (92% of the low dose and 65% of the high dose) and via faeces (14.8% of the low dose and 24.0% of the high dose). Unaltered parent

accounted for most of the excreted residue. The total radioactive residues in the daily blood and milk samples and tissues (liver, leg, loin, omental fat) were less than 0.01 mg eq./kg regardless of the treatment dose levels. In the kidney, the TRR was 0.02 mg eq./kg at a dose level of 2.1 ppm and 0.06 mg eq./kg at a dose level of 12 ppm. This was mostly imazamox (89% TRR).

CL 263284

A ruminant metabolism study was conducted with [pyridine-6-¹⁴C]-CL 263284. Dose levels for the goats, administered orally in gelatin capsules, were either 2.3 or 15 ppm daily for seven days. Samples of blood, milk and excreta were collected daily. After seven days of dosing, the goats were sacrificed (approximately 20 hours after the last dose) and the tissues kidney, liver, muscle and fat were collected.

Elimination of ¹⁴C radioactivity via faeces accounted for 82% and 68% of the total cumulative dose at the low dose and high dose, respectively. TRR levels in most tissue samples (muscle, fat, liver) from the low and high dose treated goat and all milk samples were < 0.01 mg eq./kg. The kidney showed a residue of 0.03 mg eq./kg at the 15 ppm dose, which comprised minor component CL 263284 (9% TRR, < 0.01 mg/kg) and very labile component M1 (salt or conjugate of CL 263284; 78% TRR, 0.02 mg eq./kg).

CL 312622

Lactating goats were orally treated with a mixture of [pyridine-6-¹⁴C, ¹³C]-CL 312622. The three goats were dosed for five consecutive days with either 3.1 or 33 ppm. Milk, urine and faeces samples were collected daily. Edible tissues (muscle, fat, liver and kidney) were collected at sacrifice (approximately 22 hours after the last dose).

About 90% of the total cumulative dose was excreted via the faeces. TRR levels in all tissues and milk samples were < 0.006 mg eq./kg, except kidney (0.025 mg eq./kg) and liver (0.009 mg eq./kg) of goats treated at the high dose level (33 ppm).

In the kidney sample, CL 312622 was the predominant radioactive residue (60% TRR). The impurity (CL 152795) present in the dosing solution was found at 11% of TRR. Minor polar unknowns (total 10% of TRR) and non-polar unknowns (total 12% of TRR) were also present in the kidney extract, composed with fractions of 0.003 mg eq./kg with multiple components. In the liver, CL 312622 was present at 38% of TRR (impurity, CL 152795, 19% TRR) and polar and nonpolar (31% and 11% TRR, respectively) fractions were equivalent to 0.003 mg eq./kg or lower, containing multiple components.

In summary imazamox and its metabolites (CL 263284 and CL 312622) each was mainly excreted unchanged through urine and faeces in lactating goats. There was no accumulation in any other edible goat tissue or in the milk (< 0.01 mg eq./kg) except kidney. Kidney mostly contained the unchanged administered compound.

Metabolism of imazamox in laying hens

Imazamox

Laying hens were orally dosed with [pyridine-6-¹⁴C]-imazamox at a dose level of either 2.1 or 10 ppm for seven consecutive days. Eggs were collected twice daily and blood and the tissues (liver, kidney, muscle, and skin with adhering fat) were collected for analysis approximately 22 hours after the last dose. About 85% of the total dose administered at the low and high dose was in the excreta. Residues in eggs, skin with adhering fat, muscle, liver and kidney tissues were all less than 0.01 mg eq./kg.

CL 263284

A poultry metabolism study was conducted with [pyridine-6-¹⁴C]-CL 263284. Hens were dosed orally at a dose level of either 2.1 or 11 ppm by gelatin capsules for seven days. Eggs and excreta were collected daily. The hens were sacrificed and the tissues (liver, kidney, muscle and skin with adhering fat) were collected approximately 22 hours after the last dose. About 87% of the total dose administered at the low and high dose was eliminated via excreta. Residues in all tissues and eggs were less than 0.01 mg eq./kg.

CL 312622

Laying hens were orally treated with a mixture of [pyridine-6-¹³C]-CL 312622 and [pyridine-6-¹⁴C]-CL 312622. Hens were dosed for five consecutive days with a dose level of either 0.13 or 10.5 ppm. Eggs were collected twice daily and the edible tissues (muscle, liver and skin with adhering fat) were collected at sacrifice approximately 22 hours after the last dose.

About 89% of the total dose administered at the low dose and high dose was eliminated via the excreta. Residues in tissues (liver, muscle and skin with adhering fat) and eggs were all 0.006 mg eq./kg or below. There was no retention or accumulation in eggs or edible poultry tissues.

In summary, in laying hens, imazamox, its metabolites (CL 263284 and CL 312622) were mainly eliminated unchanged through excreta. No residues (< 0.01 mg eq./kg) in eggs or edible tissues were found.

Plant metabolism

The Meeting received information on the fate of imazamox in oilseed rape, soya bean, pea, maize, wheat and alfalfa.

The metabolic fate of imazamox in imidazolinone-tolerant oilseed rape was investigated in one indoor and two outdoor studies. In one of the outdoor studies, a mixture of [pyridine-6-¹⁴C]-imazamox and [pyridine-6-¹³C]-imazamox was post-emergence treated at 0.02 kg ai/ha. Residues in plant at 0 DAT and seed at 82 DAT were 2.1 mg eq./kg and < 0.002 mg eq./kg, respectively (not further identified for component in plant and seed).

In the other two studies (indoor or outdoor), either [pyridine-6-¹⁴C]-imazamox or [imidazolinone-5-¹⁴C, 3-¹⁵N]-imazamox was applied post-emergence at rates of 0.051–0.089 kg ai/ha (outdoor) or 0.075 kg ai/ha (indoor), respectively. TRR in plant at 0 DAT were 2.2–3.9 mg eq./kg. Residues in forage (12–22 DAT) ranged from 0.04 mg eq./kg to 0.89 mg eq./kg. In straw and seed (78–90 DAT), residues were 0.088–1.1 mg eq./kg and 0.004–0.15 mg eq./kg, respectively. The majority of residues (80–99% TRR) in forage and straw samples were extracted with aqueous methanol or acidic aqueous methanol. Extractability in seeds was relatively low, 58–80% TRR.

In both labels, major components of the residues in forage were imazamox (16–42% TRR) and CL 263284 (36–54% TRR). In straw, major components were CL 263284 (44–50% TRR) and CL 312622 (up to 26% TRR); imazamox, < 2% TRR. In rape seed, major components of the residues were CL 263284 (up to 31%) or CL 189215 (up to 21%); imazamox, present at up to 13%.

The metabolic fate of [pyridine-6-¹⁴C]-imazamox in soya bean under outdoor field was studied with post-emergence treatment at a rate of 0.39 kg ai/ha. TRR in plant at 0 DAT was 55 mg eq./kg. Residues in forage (29–60 DAT) ranged from 0.13 mg eq./kg to 0.56 mg eq./kg. In straw and seed (153 DAT), residues were 0.08 mg eq./kg and 0.02 mg eq./kg, respectively. The majority of residues in forage (86–97%) were extracted with aqueous methanol and dichloromethane. Acidic and/or basic digestion for straw and seed samples extracted up to 53% and 57% of residues, respectively.

A major component of the residue in soya bean forage (29–60 DAT) was CL 189215 (32–36% TRR); imazamox, CL 263284 and CL 312622 each, present at 6–11% TRR. In soya bean seed, CL 263284 was a major component, representing 12% TRR.

Field peas were treated post-emergent, under outdoor growing conditions, with [pyridine-6-¹⁴C]-imazamox at a rate of 0.040 kg ai/ha. TRRs in whole plant at 0 DAT and 20 DAT were 1.1 mg eq./kg and 0.035 mg eq./kg, respectively. At 61 DAT, residues in all of the samples (pea foliage, immature peas, pea shells and pea pods) were < 0.01 mg eq./kg. In pea and pea hay (84 DAT), residues were 0.01 mg eq./kg and 0.05 mg eq./kg, respectively. The aqueous methanol extracted 61–99% of the TRR in whole plant. From the hay and peas, 58% and 39% of the TRR was extracted, respectively.

In pea hay, imazamox was present at 0.02 mg eq./kg (66% TRR) and other components (CL 263284, CL 189215) were negligible (\leq 0.01 mg eq./kg).

Alfalfa was treated, post-emergent, in plots at different ages of crop and timing of application under outdoor conditions with [pyridine-6-¹⁴C]-imazamox at a rate of 0.13 kg ai/ha. TRR in alfalfa plants at 0 DAT was 6.5–15 mg eq./kg. Residues in forage (26 DAT) ranged from 0.18 mg eq./kg to 0.67 mg eq./kg. Residues in forage (1st, 2nd, 3rd cut at 26–111 DAT) and hay (1st, 2nd, 3rd cut at 28–160 DAT) were < 0.01–0.21 mg eq./kg and 0.02–0.83 mg eq./kg, respectively. The majority (65–99% TRR) of residues in forage and hay were extracted with a solvent mixture of methanol/acetone/water.

Residue components in alfalfa forage (26 DAT) were: imazamox, 3–6% TRR and CL 263284, CL 189215 and CL 312622, 14–26% TRR. For forage and hay samples, 1st, 2nd, 3rd cut, composition of the compounds were similar to those in forage at 26 DAT.

The metabolic fate of imazamox on imidazolinone-tolerant maize was investigated in two outdoor studies. Radiolabelled imazamox, either [pyridine-6-¹⁴C]-imazamox or a mixture of [pyridine-6-¹⁴C]-imazamox and [pyridine-6-¹³C]-imazamox was post- or pre-emergence (one day after seedling) treated at rates of 0.13–0.14 kg ai/ha. Residues in forage (14, 30 and 62 DAT) ranged from 0.011 mg eq./kg to 0.41 mg eq./kg. In fodder and grain (100–112 DAT), TRRs were 0.012–0.047 mg eq./kg and 0.010–0.01 mg eq./kg, respectively. 40–98% of the TRR in maize samples were extracted with aqueous methanol (40% TRR in fodder).

Major components of the residues in maize forage were imazamox (18–31% TRR) and CL 263284, (12–23% TRR). In fodder, CL 263284 was present at 15% TRR, < 1–7% TRR in the other components. In grain, major components were CL 263284 (20% TRR) and CL 189215 (15% TRR) with imazamox at low level, < 5% TRR.

The metabolic fate of imazamox on imidazolinone-tolerant spring wheat was investigated under indoor and outdoor conditions. Radiolabelled imazamox, [pyridine-6-¹⁴C]-imazamox or [imidazolinone-5-¹⁴C, 3-¹⁵N]-imazamox was post-emergence applied at rates of 0.14 or 0.76 kg ai/ha. Residues in forage (8–28 DAT) ranged from 0.10 mg eq./kg to 1.6 mg eq./kg. In straw and grain (62–70 DAT), residues were ranged in 0.16–3.2 mg eq./kg and 0.067–1.4 mg eq./kg, respectively. The 53–93% TRR in all wheat samples was extracted with methanol and water or acidic aqueous methanol (53% in straw).

Major components of the residues in spring wheat forage were imazamox (42–67% TRR) and CL 263284 (10–18% TRR). In straw, CL 263284 was most abundant (13–38% TRR). The other components, imazamox (8–10% TRR), CL 189215 (3–15% TRR) and CL 312622 (6–17% TRR) were found at lower levels. In wheat grain, imazamox was most abundant component (40–70% TRR, 0.027–1.1 mg eq./kg); CL 263284 (7–10% TRR) and CL 189215 (3–4% TRR) were present at relatively low levels and CL 312622 was not detected.

The key step of the metabolism of imazamox in plant was the cleavage of the methyl ether group (demethylation) resulting in metabolite CL 263284. Subsequently, oxidation of the hydroxyl group of CL 263284 generated the dicarboxylic acid metabolite CL 312622, while glycosylation led to the glucose conjugate CL 189215.

In conclusion, in the edible portions of most treated food crops harvested at maturity, no or a very small residue of imazamox or its metabolites are expected to be found. However, for certain crops such as wheat, it is considered that the residues may be detected in wheat grain. In animal feed crops, imazamox, CL 263284, CL 189215 and CL 312622 are expected to be found above the LOQ.

Environmental fate

The Meeting received information on aerobic soil metabolism, photodegradation on the soil surface, hydrolysis and residues in succeeding crops.

Aerobic soil metabolism

Imazamox applied in sandy loam soil degraded rapidly. In three studies, half-life of imazamox was 28–38 days in sandy loam soil treated with imazamox at 0.050–0.10 kg ai/ha. However, in another study, half-life of imazamox treated in combinations of soil type (silty clay loam and silt loam) and temperature (10 °C and 20 °C) was in a range of 12–207 days (DT₉₀, 39–687 days). Imazamox was shown to be moderately persistent in aerobic soil. In all the studies, dicarboxylic acid (CL 312622) and hydroxy acid (CL 354825) metabolites were the major residue components. The parent and both metabolites were ultimately mineralized to CO₂.

Residues in succeeding crops

In a confined rotational crop study, [pyridine-6-¹⁴C]-imazamox was applied once to soya beans at the 4–6 leaf stage, in a sandy loam soil, at a rate of 0.072 kg ai/ha. One-hundred days after treatment, the soya bean crop was harvested. On the day of harvest, winter wheat was seeded into a subplot (100-day plant-back interval; PBI) of the treated field. Maize, radish, and lettuce were seeded into separate subplots at a 268-day PBI. Total radioactive residues were < 0.01 mg eq./kg in all rotational crops.

In another study, radiolabelled imazamox, either [imidazolinone-5-¹⁴C, 3-¹⁵N]-imazamox or [pyridine-3-¹⁴C, imidazolinone-3-¹⁵N]-imazamox were applied to bare sandy loam soil in plastic container followed by sowing spinach, white radish and spring wheat at PBIs of 1 month, 4 month and 1 year.

In spinach and white radish, residues were < 0.01 mg eq./kg at any PBIs. However, in spring wheat samples (forage, hay, straw, grain), total residues (TRR) were: 0.008–0.078 mg eq./kg at one month PBI (grain, 0.032–0.053 mg eq./kg), 0.004–0.132 mg eq./kg at four month PBI (grain 0.019–0.035 mg eq./kg) and < 0.001–0.052 mg eq./kg at one year PBI (grain, 0.002–0.004 mg eq./kg). In wheat grain at one month PBI, residues of imazamox and CL 263284 were 0.001–0.005 mg eq./kg.

In conclusion, residues of imazamox and the metabolites are expected to be less than 0.01 mg eq./kg in succeeding crops.

Photodegradation

Soil photolysis of [pyridine-6-¹⁴C]-imazamox was studied in a sandy loam soil, surface treated at a rate equivalent to 0.10 kg ai/ha and exposed for 30 days to artificial sunlight. The 92% imazamox at time-0 decreased to 74% imazamox at the end of the 30 days irradiation. A half-life of imazamox was calculated to be 65 days. A degradate, dicarboxylic acid CL 312622 (2% TAR in dark control), was formed at about 14% of the total residues after 30 days irradiation.

Imazamox is photodegraded with a half-life of 65 days on the surface of soil. Any degradate specific for photolysis was not found.

Hydrolysis

Imazamox is used for rice production. In the hydrolysis study under different pH conditions, imazamox was stable at pH 4, pH 7 and pH 9.

Methods of analysis

The Meeting received description and validation data for analytical methods for residue analysis of imazamox and its metabolites in various plant and animal commodities.

In general, the methods involved extraction of residues with acidic methanol-water solution, clean-up procedure by mainly solvent partitioning and solid phase extraction, and determination by HPLC-UV or LC-MS/MS. In the case of milk and fat, acetonitrile in hexane is used for the extraction step. Some methods employ capillary electrophoresis-UV or GC-NPD, in case of use of GC-NPD, where combined determination for imazamox-related residues is possible by converting to a common methylated product.

A number of specific methods for plant matrices were found suitable for analysis of imazamox, CL 263284, CL 189215 and CL 312622 with LOQ ranging 0.01–0.05 mg/kg for these analytes except that it was 0.1 mg/kg for alfalfa.

For animal matrices, one method determined by LC-MS/MS was submitted and found suitable for analysis of imazamox and CL 263284 with LOQs of 0.01 mg/kg for bovine matrices and poultry egg.

No multi-residue methods were submitted.

Stability of residues in stored analytical samples

The stability of imazamox and its metabolites during frozen storage of samples was investigated in a range of plant matrices for which supervised residue trials were submitted.

Compounds tested were imazamox, CL 263284, CL 189215 and CL 312622. Each compound was spiked to matrices at 0.1 to 1 mg/kg.

All of the compounds tested were found to be stable (> 70% remaining) at least during the storage periods tested: for imazamox, 3.6 years in soya bean (seed, forage and hay), 4 years in wheat (grain, straw, forage and hay), 2 years in maize (grain, ear and immature plant), 1.5 years in rape seed and 1.5 years in alfalfa (hay, forage and seed); for CL 263284, 3.6 years in soya bean (seed, forage and hay), 10 months in processed soya bean products, 4 years in wheat (grain, straw, forage and hay), 2 years in maize (grain, ear and immature plant) and peanut (hull and nutmeat) and 1.5 years in alfalfa (hay, forage and seed); for CL 189215, 10 months in soya bean seed and processed soya bean products, 2 years in peanut (hull and nutmeat) and 1.5 years in alfalfa (hay, forage and seed); and for CL 312622, 1.5 years in alfalfa (hay, forage and seed).

Definition of the residue

In metabolism studies of imazamox and the metabolites (CL 263284, CL 312622) in goats and hens, the compounds were mostly excreted (85–106%) unchanged through urine and faeces. In hen, no detectable residues were found in eggs or edible tissue. In goat, there were no detectable residues in milk and tissues except kidney. Residue in the kidney was predominantly the administered parent. Therefore, no residues of imazamox and related compounds are expected in livestock tissues, milk or eggs at expected livestock dietary burdens of less than 3 ppm.

The log P_{ow} for imazamox is 0.73 suggesting imazamox residues are not fat soluble.

In confined crop rotation studies, any imazamox related residues in succeeding crops were not detected above more than 0.01 mg/kg.

In primary crops, imazamox is either not found or found at very low levels (< 30% TRR, < 0.01 mg eq./kg) in non-tolerant food commodities and imidazolinone-tolerant food commodities (tolerant rape seeds, soya bean seeds, pea seeds, alfalfa, tolerant maize seeds). Imidazolinone-tolerant wheat grain, is the only food commodity, where parent is found at significant levels (40–74% TRR, 0.027–1.1 mg eq./kg). Among the metabolites found, CL 263284 is the most predominant metabolite, although present at low levels in food commodities (up to 31% TRR, maximum 0.092 mg eq./kg). In supervised trials imazamox and CL 263284 are found at levels above the LOQ in food commodities (lentil seeds, sunflower seeds). In feed commodities (tolerant rape forage or straw, soya forage or straw, pea forage or hay, alfalfa forage or hay, tolerant maize forage or fodder, wheat forage, hay or straw), imazamox (1.5–67% TRR, < 0.01–5.0 mg eq./kg) and CL 263284 are more prominent (8–54% TRR, < 0.01–1.9 mg eq./kg).

Parent and CL 263284 are the only two compounds expected to be found in food commodities. Metabolite CL 263284 can also arise in plant commodities as a result of treatment with imazapic, another imidazolinone herbicide. Since CL 263284 cannot be seen as a marker for imazamox, the Meeting decided to define the residue for enforcement/monitoring as parent only.

Parent and CL 263284 are considered relevant for dietary risk assessment as the toxicity of CL 263284 is similar to that of imazamox in rat. Therefore, the Meeting decided to define the residue for dietary risk assessment as the sum of parent and CL 263284, expressed as imazamox.

The Meeting agreed the following residue definitions:

Definition of the residue for plant and animal commodities for compliance with the MRL: *imazamox*.

Definition of the residue for plant and animal commodities for the estimation of dietary intake: *sum of imazamox and 5-(hydroxymethyl)-2-(4-isopropyl-4-methyl-5-oxo-2-imazazolin-2-yl) nicotinic acid (CL 263284), expressed as imazamox*.

Residue is not fat-soluble.

Should imazamox be used on crops other than cereals, pulses and oilseeds, the residue definition may need to be revised.

Results of supervised residue trials on crops

The Meeting received supervised trial data for imazamox on legume vegetables (beans and peas), pulses (bean, pea, lentil and soya bean), cereals (rice and wheat), oil seed crops (peanut, rape and sunflower) and alfalfa.

In below, a maximum residue level was estimated based on residue concentration of imazamox. Total residue means sum of parent compound and CL 263284. Concentration of CL 263284 was expressed as parent equivalents (conversion factor, 1.048).

Legume vegetables

Beans

Residue trials on beans were performed in Denmark, Germany, France, the UK, Greece, Italy, Spain and the USA. The GAP for beans in Chile is a single early post-emergent application at 0.056 kg ai/ha with no PHI specified.

In six trials on French beans conducted in Italy (1 × 0.050 kg ai/ha at post-emergence) matching the Chile GAP, residues in bean pods with seeds were: parent < 0.05 (6) mg/kg and metabolite < 0.05 (6) mg/kg. Total residues in the bean pods with seeds were (n=6): < 0.1 (6) mg/kg.

In other six trials from USA (1×0.050 kg ai/ha at post-emergence) matching the Chile GAP, residue concentrations of imazamox (only measured) were < 0.05 (6) mg/kg in pods with seeds of snap beans.

Three trials conducted in France, the UK and Italy involved an earlier application timing and a higher rate (1×0.075 kg ai/ha at pre-emergence). Residues in pods with seeds of common bean (flageolet bean) were: parent < 0.01 (3) mg/kg, metabolite < 0.01 (3) mg/kg. Total residues in the bean pods with seeds were < 0.02 (3) mg/kg.

The Meeting considered that there was no expectation of residues above LOQ in bean pods with seeds. The Meeting estimated a maximum residue level of 0.05^* mg/kg and an STMR of 0 mg/kg for beans, except broad bean and soya bean (green pods and immature seeds).

Peas

Residue trials on peas were performed in Italy, France, Spain, the UK, Germany and the USA. The GAP for peas in France is for a single pre-emergent application post sowing per every 2 years, treating on soil at 0.075 kg ai/ha with a PHI of 63 days.

In nine trials conducted in Italy and France approximating the French GAP (1×0.068 – 0.075 kg ai/ha at pre-emergence, 70–110 day PHI), residues in pea seeds were: parent < 0.05 (9) mg/kg and metabolite < 0.05 (9) mg/kg. Total residues in pea seeds were (n=9): < 0.1 (9) mg/kg.

Another ten trials were conducted in Italy and Spain with post-emergence treatments at 0.050 – 0.052 kg ai/ha in eight trials and 0.073 – 0.075 kg ai/ha in two trials. The total residues were all < 0.1 (10) mg/kg.

The Meeting estimated a maximum residue level of 0.05^* mg/kg and an STMR of 0 mg/kg for peas, shelled (succulent seeds).

Pulses

Bean (dry)

Residue trials on dry beans were performed in France, Germany, Netherlands, the UK, Italy, Greece, Spain and the USA. The GAP for dry bean in the UK is a single pre-emergence application to soil at a rate of 0.075 kg ai/ha.

In four trials from France, the UK and Italy (1×0.075 kg ai/ha at pre-emergence, 91–108 day PHIs), approximating the UK GAP, residues in common bean seeds were: parent < 0.01 (4) mg/kg and metabolite < 0.01 (4) mg/kg. Total residues in seed of common beans were < 0.02 (4) mg/kg. In these trials, the total residues in whole plants harvested early (PHIs of 32–48 days) were < 0.02 mg/kg.

In two trials from the USA applied at a post-emergence timing and at a rate comparable to the UK GAP (1×0.070 kg ai/ha, 61–98 day PHIs), residue concentrations of the parent compound were also below LOQ, < 0.05 (2) mg/kg.

Pea (dry)

The GAP for dry peas in France is a single pre- or post-emergence application every 2 years at a rate of 0.075 kg ai/ha with a PHI of 63 days. A total of ten trials were conducted in France at the GAP rate (1×0.075 kg ai/ha at pre-emergence) but with longer PHIs (106–129 days). The residues measured for each compound or combined total residue were: parent < 0.05 (5) mg/kg, metabolite < 0.05 (5) mg/kg and total residue < 0.1 (10) mg/kg.

Lentil (dry)

Residue trials for lentil were available from Canada and the USA. In Canada, imazamox is approved for use in imidazolinone-tolerant lentils with a single early post-emergent application at a rate of 0.020 kg ai/ha (plus adjuvant) with a PHI of 60 days.

In a total of fourteen trials (1×0.015 – 0.021 kg ai/ha at post- or early post-emergent timings and a 60 day, or shorter, PHI (without use of an adjuvant), residues in imidazolinone-tolerant lentils were: imazamox < 0.05 (9), 0.056, 0.060, 0.065, 0.12, 0.12 mg/kg and metabolite < 0.05 (14) mg/kg. Total residues were: < 0.1 (9), 0.11 (3), 0.17, 0.17 mg/kg.

Soya bean (dry)

Residue trials on soya bean were performed in France, Germany, Italy and Canada. The GAP for soya bean in Brazil is for a single post-emergence application at a rate of 0.049 kg ai/ha (plus adjuvant) with a PHI of 70 days.

In nine trials conducted in France, Germany and Italy (1×0.042 – 0.045 kg ai/ha at post- or early post-emergence, 69–104 days of PHI, with or without adjuvant) approximating the Brazilian GAP, residues in soya bean seeds were: imazamox < 0.01 (7) mg/kg and metabolite < 0.01 (7) mg/kg. Total residues were < 0.02 (7) mg/kg. Of which five trials showed no effect of adjuvant on the level of residue in dry seed.

In two trials conducted in Canada at an exaggerated rate of 0.070–0.071 kg ai/ha (single post-emergence application, 106–112 day PHIs), total residues were all < 0.05 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.05* mg/kg and an STMR of 0 mg/kg for bean and pea in dry, respectively.

For lentil (dry), the Meeting estimated a maximum residue level of 0.2 mg/kg and an STMR of 0.1 mg/kg.

For soya bean (dry), the Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR of 0 mg/kg.

*Cereals**Rice*

Residue trials on imidazolinone-tolerant rice were performed in Italy and Spain. The use pattern in Spain is twice post-emergence treatment at a rate of 0.035 kg ai/ha with an interval of 14–21 days and no PHI, applying on imidazolinone-tolerant rice plant in water or dry planted.

In a total of six trials on imidazolinone-tolerant rice (2×0.035 – 0.038 kg ai/ha at BBCH 13–14 and BBCH 25–31, 10–12 day interval) from Italy and Spain matching the Spain GAP, residues in rice grain were: imazamox < 0.01 (6) mg/kg and metabolite < 0.01 (3), 0.02, 0.03 (2) mg/kg. Total residues were: < 0.02 (3), 0.030, 0.040 (2) mg/kg.

The Meeting estimated a maximum residue level of 0.01* mg/kg and an STMR of 0.025 mg/kg for rice.

Wheat

Residue trials on imidazolinone-tolerant wheat were performed in France, Italy, Canada and the USA. The GAP for wheat (imidazolinone-tolerant) in Argentina is a single early post-emergence application at 0.070 kg ai/ha with no PHI.

In a total of twelve trials from France (eight trials), Italy (four trials) and USA (one trial) (1×0.067 – 0.075 kg ai/ha at post-emergence) matching the GAP, residues in imidazolinone-tolerant wheat grain were: imazamox < 0.05 (13) mg/kg and metabolite < 0.05 (13) mg/kg. Total residues were < 0.1 (13) mg/kg.

The Meeting considered that there is no expectation of residues above the LOQ for wheat grain and agreed to estimate a maximum level of 0.05^* mg/kg and an STMR of 0.1 mg/kg for wheat.

Oilseeds

Peanuts

Five trials were conducted in Brazil with a single post-emergence application (BBCH 71–79) at a rate of 0.056 kg ai/ha with a PHI of 43–50 days without use of an adjuvant, matching the GAP for peanut in South Africa (1×0.048 kg ai/ha plus adjuvant) at post-emergence with a PHI 50 days. The residues in peanut kernels were: imazamox < 0.01 (5) mg/kg and metabolite < 0.01 (5) mg/kg. Total residues were < 0.02 (5) mg/kg.

Although only a relatively small number of trials were available, there is no expectation of residues above the LOQ in peanuts. The Meeting estimated a maximum residue level of 0.01^* mg/kg and an STMR of 0 mg/kg.

Rape seed

Residue trials on imidazolinone-tolerant oilseed rape were conducted in France, Germany, the UK and Canada and Argentina. The GAP for imidazolinone-tolerant rape in Chile is a single early post-emergence application at a rate of 0.056 kg ai/ha with no PHI. In six trials from Germany, France and Argentina (1×0.050 kg ai/ha at post-emergence) matching the Chile GAP, residues in rape seed (imidazolinone-tolerant variety) were: imazamox < 0.01 (2), < 0.05 (4) mg/kg and metabolite < 0.01 (2), < 0.05 (4) mg/kg. Total residues were < 0.02 (2), < 0.1 (4) mg/kg.

In another eighteen trials from France, Germany and the UK, an exaggerated rate of 0.073 – 0.079 kg ai/ha did not lead to above LOQ (< 0.05 mg/kg) for total residues in seeds of imidazolinone-tolerant oilseed rape.

The Meeting considered that there is no expectation of residues above the LOQ in rape seeds.

The Meeting estimated a maximum residue level of 0.05^* mg/kg, an STMR of 0 mg/kg for rape seed.

Sunflower seed

Residue trials on imidazolinone-tolerant sunflower were conducted in France, Germany, UK, Italy, Spain, Argentina, Canada and USA. In Canada, critical GAP for sunflower (imidazolinone-tolerant) is a single early post-emergence application at a rate of 0.015 kg ai/ha with a specified PHI of 60 days and an addition of adjuvant.

A total of six trials conducted in Canada and USA (1×0.015 – 0.019 kg ai/ha at PHIs of 58–68 days with or without adjuvant) approximated the Canadian GAP. The residues in seeds of imidazolinone-tolerant sunflower were: imazamox < 0.05 (2), 0.05 (2), 0.07, 0.14 mg/kg and metabolite < 0.05 , 0.06, 0.10, 0.16, 0.17, 0.19 mg/kg. Total residues were: < 0.1 , 0.13, 0.15, 0.22, 0.25, 0.30 mg/kg.

The Meeting estimated a maximum residue level of 0.3 mg/kg and an STMR of 0.19 mg/kg for sunflower seed.

*Legume animal feeds**Alfalfa*

Residue trials on alfalfa were performed in Greece, Spain and USA. The GAP for alfalfa in France is a single post-emergence application at a rate of 0.067 kg ai/ha with a PHI of 30 days.

In a total of seven trials from Greece, Spain and USA (1×0.067 – 0.075 kg ai/ha at PHIs of 26–30 days) matching the French GAP, residues in alfalfa forage were as received basis: imazamox < 0.1 (7) mg/kg and metabolite < 0.1 (7) mg/kg. Total residues in alfalfa forage were < 0.2 (7) mg/kg. For alfalfa hay, residues were as received basis: imazamox < 0.1 (5) mg/kg and metabolite < 0.1 (3), 0.19, 0.29 mg/kg. Total residues were < 0.2 (3), 0.32, 0.41 mg/kg in hay.

The Meeting estimated a median residue of 0 mg/kg and a highest residue of 0.2 mg/kg for alfalfa forage.

For alfalfa hay, the Meeting estimated a maximum residue level of 0.1* mg/kg, a median residue of 0.20 mg/kg and a highest residue of 0.41 mg/kg.

Pea vines (green) and pea fodder

Five trials approximating the French GAP for pea (single pre-emergence post-sowing per every 2 years at 0.075 kg ai/ha) were conducted in France with PHIs of 88–110 days. Residues in pea vines, (pods + haulm) on an as received basis, were: imazamox < 0.05 (5) mg/kg and metabolite < 0.05 (5) mg/kg. Total residues in pea vines were < 0.1 mg/kg.

Ten trials approximating the French GAP for field pea (single pre- or post-emergence application per every 2 years at a rate of 0.075 kg ai/ha) were conducted in France with PHIs of 106–120 days. Residues in pea fodder (straw or pods + haulm) on an as received basis, were: imazamox < 0.05 (5) mg/kg and metabolite < 0.05 (4), 0.17 mg/kg. Total residues were < 0.05 (5), < 0.1(4) and 0.22 mg/kg.

The Meeting estimated a median residue of 0.1 mg/kg and a highest residue of 0.1 mg/kg for pea vines. For pea fodder, the Meeting estimated a maximum residue level of 0.05* mg/kg, a median residue of 0.075 mg/kg and a highest residue of 0.22 mg/kg.

Soya bean, forage and fodder

Four trials were conducted in France and Germany approximating the Brazil GAP for soya bean (1×0.049 kg ai/ha). Residues in soya bean forage harvested at 27–28 PHIs were as received basis: imazamox < 0.01 (4) mg/kg and metabolite < 0.01 (4) mg/kg. Total residues were < 0.02 (4) mg/kg. For fodder, residues were as received basis: imazamox < 0.01 (4) mg/kg and metabolite < 0.01 (2), 0.01, 0.05 mg/kg. Total residues were < 0.02 (2), 0.02, 0.06 mg/kg in soya bean fodder.

For soya bean forage, the Meeting estimated a median residue of 0.02 mg/kg and a highest residue of 0.02 mg/kg.

For soya bean fodder, the Meeting estimated a maximum residue level of 0.01* mg/kg, a median residue of 0.02 mg/kg and a highest residue of 0.06 mg/kg.

*Forage and fodder of cereal grains and grasses**Rice straw and fodder*

In six trials conducted in Italy and Spain matching the Spain GAP (post-emergence treatment on imidazolinone-tolerant rice plant, water or dry planted, 2×0.035 kg ai/ha, 14–21 day interval), residues in imidazolinone-tolerant rice straw (77–90 day PHIs) were as received basis: imazamox

< 0.01 (6); metabolite < 0.01 (3), 0.01, 0.02 (2) mg/kg. Total residues were < 0.02 (3), 0.02, 0.03 (2) mg/kg in straw.

The Meeting estimated a maximum residue level of 0.01* mg/kg, a median residue of 0.02 mg/kg and a highest residue of 0.03 mg/kg in rice straw.

Wheat forage and straw

Trials on imidazolinone-tolerant wheat were conducted in Canada approximating the GAP for imidazolinone-tolerant wheat in Canada (single early post-emergence application at 0.020 kg ai/ha). In Canada, grazing and cutting for hay are not permitted within 4 days and 42 days of application, respectively. Five trials for forage (7, 14 day PHIs) and four trials (42, 56 day PHIs) for hay and five trials (72–90 PHIs) for straw matched the Canadian GAP on feedstuffs.

Residues in imidazolinone-tolerant wheat forage were as received basis: imazamox < 0.05 (2), 0.05, 0.13, 0.15 mg/kg; metabolite < 0.05 (5) mg/kg. Total residues were < 0.1 (2), 0.10, 0.20, 0.23 mg/kg.

Residues in imidazolinone-tolerant wheat hay were as received basis: imazamox < 0.05 (4) mg/kg; metabolite < 0.05 (4) mg/kg. Total residues were < 0.1 (4) mg/kg.

Residues in imidazolinone-tolerant wheat straw were as received basis: imazamox < 0.05 (5) mg/kg; metabolite < 0.05 (5) mg/kg. Total residues were < 0.1 (5) mg/kg.

For wheat forage, the Meeting estimated a median residue of 0.1 mg/kg and a highest residue of 0.23 mg/kg.

For wheat hay and straw, the Meeting estimated a maximum residue level of 0.05* mg/kg, a median residue of 0 mg/kg and a highest residue of 0.1 mg/kg.

Miscellaneous Fodder and Forage crops

Rape seed forage

In four residue trials on imidazolinone-tolerant oilseed rape conducted in France and Germany, matching the GAP of Chile for oilseed rape (imidazolinone-tolerant rape, a single early post-emergence application, 0.056 kg ai/ha), residues in whole plants without roots (12–19 day PHIs) on an as received basis were: imazamox, 0.05, 0.12, 0.14 0.19 mg/kg; metabolite 0.52, < 0.05, 0.21, 0.28 mg/kg. Total residues were: 0.10, 0.33, 0.42 and 0.71, mg/kg.

The Meeting estimated a median residue of 0.38 mg/kg and a highest residue of 0.71 mg/kg for rape forage.

Fate of residues during processing

High temperature hydrolysis

The hydrolysis of [pyridine-3-¹⁴C, imidazolinone-3-¹⁵N]-imazamox was investigated in aqueous buffer solutions. After pasteurization (20 minutes at 90 °C, pH 4), baking/brewing/boiling (60 minutes at 100 °C, pH 5) and sterilization (20 minutes at 120 °C, pH 6), 98–104% of the applied radioactivity remained in the test solutions, where the detectable radioactive component was unchanged imazamox only. Imazamox was stable under such simulated processing conditions.

Processing

Information on processing of wheat and sunflower seed were available for an estimation of maximum residue level and STMR-P for the processed product. Estimated processing factors, maximum residue

levels and STMR-Ps are summarized below. A maximum residue level and STMR-P value for processed product were calculated with imazamox residue and STMR value (total residue of imazamox and CL 263284), respectively.

RAC and processed product	RAC		Pf, best estimate (individual Pf)		Processed product	
	Estimated maximum residue level (mg imazamox/kg)	STMR (mg total/kg)	Imazamox	Total residue	Estimated maximum residue level (mg imazamox/kg)	STMR-P total residue (mg total/kg)
Wheat	0.05*	0.1				
Wheat germ			2.7	2.2	0.1	0.22
Wheat bran, unprocessed			3.9	3.4	0.2	0.34
Wheat flour			1.2	1.2	0.06	0.12
Wheat asp. grain fraction			1.0	1.0		0.10
Wheat by products (middling, shorts)			2.4 (1.6, 3.2)	2.1 (1.5, 2.6)		0.21
Sunflower seed	0.3	0.19				
Sunflower seed meal			2.3	2.5 (1.9, 3.0)		0.48
Sunflower refined oil				< 0.5 (< 0.2, < 0.5)		0.095

The Meeting estimated maximum residue levels of 0.1 mg/kg for wheat germ and 0.2 mg/kg for wheat bran, unprocessed.

Residues in animal commodities

Farm animal feeding studies

Information on farm animal feeding studies was not submitted.

Estimation of dietary burdens

Dietary burden calculations for beef cattle and dairy cattle and poultry are provided below. The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2009 edition of the FAO Manual.

Summary of livestock dietary burden (ppm of dry matter diet)

	US-Canada		EU		Australia		Japan	
	max	mean	max	mean	max	mean	max	mean
Beef cattle	0.230	0.178	0.821	0.463	2.37 ^a	1.27 ^c	0.217	0.193
Dairy cattle	0.670	0.404	0.0749	0.0433	1.50 ^b	0.765 ^d	0.256	0.197
Poultry broiler	0.278	0.278	0.179	0.179	0.200	0.200	0.052	0.023
Poultry layer	0.278	0.278	0.75 ^e	0.478 ^f	0.188	0.188	0.072	0.072

^a Highest maximum beef cattle dietary burden suitable for MRL estimates for mammalian meat

^b Highest maximum dairy cattle dietary burden suitable for MRL estimates for milk

^c Highest mean beef cattle dietary burden suitable for STMR estimates for mammalian meat

^d Highest mean dairy cattle dietary burden suitable for STMR estimates for milk

^e Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs.

^f Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs

Animal commodity maximum residue levels

Maximum estimated dietary burdens for beef cattle and dairy cattle were 1.4 and 1.1 ppm, respectively. These dietary burdens were similar to the dose rates in the metabolism studies in lactating goats (< 0.01 mg eq./kg at 2.1 ppm for imazamox; < 0.01 mg eq./kg at 2.3 ppm for CL 263284). As no residues in cattle meat and milk are expected, the Meeting estimated a maximum residue level of 0.01* mg/kg and HR and STMR of 0 in each animal commodity: milk, meat (mammalian except marine mammals) and edible offal and fat.

In poultry, the maximum dietary burden, 0.75 ppm was 3 times lower than dose rates in metabolism studies in laying hens (< 0.01 mg eq./kg at 2.1 ppm for imazamox and CL 263284 each). The Meeting estimated a maximum residue level of 0.01* mg/kg and HR and STMR of 0 for poultry meat, poultry edible offal, poultry fat and eggs.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed below are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue for plant and animal commodities for compliance with the MRL:
imazamox

Definition of the residue for plant and animal commodities for estimation of dietary intake:
sum of imazamox and 5-(hydroxymethyl)-2-(4-isopropyl-4-methyl-5-oxo-2-imazazolin-2-yl) nicotinic acid (CL 263284), expressed as imazamox

Residue is not fat soluble.

DIETARY RISK ASSESSMENT***Long-term intake***

The ADI for imazamox is 0–3 mg/kg bw. The International Estimated Daily Intakes (IEDIs) for imazamox were estimated for the 17 GEMS/Food Consumption Cluster Diets using the STMR or STMR-P values estimated by the present JMPR. The results are shown in Annex 3 of the 2014 JMPR Report. The IEDIs were 0% of the maximum ADI. The Meeting concluded that the long-term intake of residues of imazamox from uses considered by the JMPR is unlikely to present a public health concern.

Short-term intake

The ARfD for imazamox is 3 mg/kg bw. The International Estimate of Short Term Intakes (IESTIs) for imazamox were calculated for the food commodities for which STMRs or HRs were estimated by the present Meeting and for which consumption data were available. The results are shown in Annex 4. The IESTIs were 0% of the ARfD for children and the general population.

The Meeting concluded that the short-term intake of residues of imazamox from uses considered by the present Meeting are unlikely to present a public health concern.

