

IMAZAPIC (266)

First draft prepared by Dr Yukiko Yamada, Ministry of Agriculture, Forestry and Fisheries, Tokyo, Japan

EXPLANATION

Imazapic is an imidazolinone herbicide developed for the control of grasses and broadleaf weeds in a variety of crops. It was first reviewed by the Meeting in 2013. The 2013 JMPR decided the following residue definition and toxicological endpoints:

Definition of the residue for plant and animal commodities (for compliance with MRLs and for estimation of dietary intakes): Imazapic

Residue is not fat-soluble.

The ADI is 0–0.7 mg/kg bw and an ARfD is unnecessary.

The 2013 JMPR received and considered the plant metabolism study and supervised residue trials on transgenic soya beans; and analytical methods, storage stability studies and processing studies on soya beans. However, at the time of the 2013 JMPR, no GAP had been approved for soya bean crops, regardless of whether they are transgenic or not. Due to the lack of approved GAP, it was not possible for the Meeting to estimate maximum residue level for soya beans.

Imazapic was included on the priority list by the CCPR at the 46th Session in 2014 for evaluation for additional MRLs by this Meeting. The current Meeting received information on use patterns now approved in Brazil. The supervised trial data provided to the 2013 Meeting are now reviewed on the basis of the new use pattern.

USE PATTERNS

Imazapic is used to control broad leaf and grassy weeds. It is formulated as a liquid or granular product either as a solo product or in combination with other active substances for use on pulses, cereal grains, grasses for sugar, oilseeds, and straw, forage and fodder of cereal grains. The use of imazapic, in combination with imazapyr, has been approved in Brazil only for soya bean cultivars resistant to imidazolinone herbicides as shown below.

Table 1 Registered use of imazapic relevant to the residue evaluation by the current Meeting.

Country	Formulation Type and g/kg ^a (Other active ingredient)	F/G/P	Application rate				PHI days	Notes Timing
			Method	No. per crop and season	Water L/ha ^{2/}	Rate kg ai/ha ^b		
Pulses: Soya bean								
Brazil	WG 175 (imazapyr)	F	Ground spraying	1	100-200	0.014 - 0.0175	60	Apply only for soya bean cultivars tolerant to imidazolinone herbicides. Early to normal post-emergence of infesting weeds
Brazil	WG 175 (imazapyr)	F	Aerial spraying	1	40-50	0.014 - 0.0175	60	

^a In acid equivalents.

^b Calculated from the dose of the formulation on the label and concentration of the active ingredient (acid equivalents) in the formulation.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

The 2013 Meeting received residue data from supervised field trials conducted in Brazil on soya bean cultivars tolerant to imidazolinone herbicides, which were summarized in the Evaluation of the 2013 JMPR and reproduced here with some editorial modification, such as information on the analytical methods and storage, and additional information related to the application of imazapic.

Application rates and residue concentrations were reported as imazapic acid equivalents. Residue concentrations are recorded unadjusted for recoveries or for residue values in control samples.

Where multiple samples were taken from a single plot, individual results are reported, and the calculated average concentration is used for estimation of maximum residue level. Where trials were conducted in the same location, with the same or similar varieties, same or similar formulations, and same equipment, and at the same or similar timing, they are not regarded as independent and only the higher(est) result from these trials was chosen for the estimation of a maximum residue level. Residues from the trials conducted according to maximum GAP have been used for the estimation of maximum residue levels and they are underlined.

Soya beans

The formulation containing imazapic and imazapyr was approved in Brazil for use only on soya bean cultivars tolerant to imidazolinone herbicides. The following trials were conducted on GM soya bean cultivars to which the mutated AHAS gene (CSR1-2) of *Arabidopsis thaliana* was introduced for imidazolinone tolerance.

During the 2006/2007 growing season, eight field trials were carried out in Brazil to determine the residues levels of imazapic in soya bean after treatment with a mixed WG formulation of imazapic and imazapyr. In all trial sites, one trial plot was untreated to provide control samples and one trial plot received one post-emergence application at a rate of 0.0175 kg imazapic/ha (and 0.0525 kg imazapyr/ha) 60 days before harvest (BBCH 24-75). In three trials, the application was performed 40, 60, 80, 100 and 120 days before harvest, each on a separate plot. Samples were taken 60 days after the application (DALA) in all trials; but in three trials, additional samplings were performed 40, 80, 100 and 120 DALA. The soya bean samples were stored frozen until analysis. Soya bean samples were analysed for imazapic using Method SOP-PA.0249.

During the 2007/2008 growing season, a field trial was carried out in Brazil to determine the residues levels of imazapic in soya bean after treatment with a mixed formulation of imazapic and imazapyr. One trial plot was untreated to provide control samples, and one trial plot received one foliar post-emergence spray application at a rate of 0.0175 kg imazapic/ha (and 0.0525 kg imazapyr/ha), either 40, 60, 80, 100 or 120 days before harvest. Samples were taken 40, 60, 80, 100 or 120 days after the application. The soya bean samples were analysed for imazapic and the two metabolites using Method SOP-PA.0288.

During the 2010 growing season, two field trials were carried out in Brazil to determine the residues levels of imazapic in soya bean after treatment with a mixed formulation of imazapic and imazapyr. At both trial sites, one trial plot was untreated to provide control samples and four trial plots received one foliar post-emergence spray application at a rate of 0.0175 kg imazapic/ha (and 0.0525 kg imazapyr/ha), 20, 40, 60 or 80 days before harvest. Samples of soya bean grain were taken 20, 40, 60 and 80 days after the application. Soya bean samples were analysed for residues using Method SOP-PA.0288.

During the 2011 growing season, five field trials were carried out in Brazil to determine the residues levels of imazapic in transgenic soya bean after treatment with a mixed formulation of imazapic and imazapyr. At all trial sites, one trial plot was untreated to provide control samples, and one trial plot received one post-emergence application at a rate of 0.0175 kg imazapic/ha (and 0.0525 kg imazapyr/ha), 60 days before harvest (BBCH 66-73). At one trial with five plots, the application was performed 20, 40, 60, 80 and 100 days before harvest. Samples of soya bean grain were taken 60 days after the application (DALA) at all trials; at one trial, additional samplings were performed 20, 40, 80 and 100 DALA, and at one trial aspirated grain fractions were also sampled. Soya bean samples were analysed for residues using Method SOP-PA.0288.

Table 2 Residues of imazapic in imidazolinone-tolerant soya beans from supervised trials conducted in Brazil

Year Location (Variety)	Application rate				DALT (days)	Imazapic (mg/kg)	Study code Doc ID (Trial No.) BBCH at harvest
	Method	Rate kg ai/ha	No. date	Timing BBCH			
GAP in Brazil	Ground spray	0.014- 0.0175	1		PHI 60		
	Aerial spray	0.014- 0.0175	1		PHI 60		
2006/2007 Santo Antonio de Posse, Sao Paulo (CV 603)	n.r.	0.0175	1 19.02.07 30.01.07 10.01.07 21.12.06 01.12.06	78 72 65 53 38	40 60 80 100 120	0.08 < 0.05 < 0.05 < 0.05 < 0.05	RF-1088-06 2008/1097470 ^a (EC-CD-BRUA/ 1088-06) BBCH 89
2006/2007 Santo Antonio de Posse, Sao Paulo (CV 603)	n.r.	0.0175	1 30.01.07	24 ^b	60	< 0.05	RF-1088-06 2008/1097470 (EC-R-BRUA/ 1088-06) BBCH 89
2006/2007 Santo Antonio de Goias, Goias (CV 603)	n.r.	0.0175	1 25.02.07 05.02.07 16.01.07 27.12.06 07.12.06	77 71 66 59 39	40 60 80 100 120	0.15 0.08 < 0.05 < 0.05 < 0.05	RF-1088-06 2008/1097470 (EC-CD-BRUB/ 1088-06) BBCH 97
2006/2007 Santo Antonio de Goias, Goias (CV 603)	n.r.	0.0175	1 05.02.07	71	60	0.15	RF-1088-06 2008/1097470 (EC-R-BRUB/ 1088-06) BBCH 97
2006/2007 Brasilia Distrito Federal do Brasil (CV 603)	n.r.	0.0175	1 09.02.07	75	60	0.10	RF-1088-06 2008/1097470 (EC-R-BRUC/ 1088-06) BBCH 97
2006/2007 Uberaba, Minas Gerais (CV 603)	n.r.	0.0175	1 04.03.07 13.02.07 23.01.07 03.01.07 14.12.06	77 73 51 29 19	40 60 80 100 120	0.19 0.23 < 0.05 < 0.05 < 0.05	RF-1088-06 2008/1097470 (EC-CD-BRVA/ 1088-06) BBCH 97
2006/2007 Uberaba, Minas Gerais (CV 603)	n.r.	0.0175	1 13.02.07	73	60	0.25	RF-1088-06 2008/1097470 (EC-R-BRVA/ 1088-06) BBCH 97
2006/2007 Londrina, Parana (CV 603)	n.r.	0.0175	1 03.01.07	67	60	< 0.05	RF-1088-06 2008/1097470 (EC-R-BRTA/ 1088-06) BBCH 86
2007/2008 Santo Antonio de Posse, Sao Paulo (CV 127)	spray	0.0175	1 13.02.08 24.01.08 04.01.08 15.12.07 25.11.07	n.r. ^c 75 66 51 13	40 60 80 100 120	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01	1273-07 2010/1010261 2010/1079212 (G080102) BBCH 86 Storage: 613 d
2010	spray	0.0175	1				324476

Year Location (Variety)	Application rate				DALT (days)	Imazapic (mg/kg)	Study code Doc ID (Trial No.) BBCH at harvest
	Method	Rate kg ai/ha	No. date	Timing BBCH			
Ponta Grossa, Parana (L 08)			24.03.10	83	20	< 0.01	2010/1127505 (G100005) BBCH 91
			04.03.10	75	40	0.02	
			12.02.10	68	60	0.07	
			23.01.10	66	80	0.03	
2010 Santo Antonio de Posse, Sao Paulo (CV 127)	spray	0.0175	1				324476
			13.05.10	89	20	< 0.01	2010/1127505
			23.04.10	87	40	< 0.01	(G100006)
			04.04.10	77	60	0.05	BBCH 89
2011 Ponta Grossa, Parana (BRZ 08 200151)	spray	0.0175	1				324447
			20.05.11	79	20	< 0.01	2012/3000423
			30.04.11	75	40	< 0.01	(G100575)
			10.04.11	73	60	0.05	BBCH 83
			21.03.11	64	80	0.12	
01.03.11	62	100	< 0.01				
2011 Senador Canedo, Goias (BRZ 5384)	spray	0.0175	1				324447
			31.01.11	66	60	< 0.01	2012/3000423 (G100576) BBCH 87
2011 Anapolis, Goias (BRZ 5384)	spray	0.0177	1				324447
			04.02.11	69	60	< 0.01	2012/3000423 (G100577) BBCH 85
2011 Santo Antonio de Posse, Sao Paulo (BRZ 08)	spray	0.0175	1				324447
			12.05.11	73	60	0.23	2012/3000423 (G100578) BBCH 89
2011 Castro, Parana (BRZ 08 200151)	spray	0.0175	1				324447
			22.04.11	71	60	0.07	2012/3000423 (G100579) BBCH 83

^a Amendment to Doc ID. 2007/1065863

^b Unlikely value.

^c From the stage at the time of application for 60 DALA and the stage at harvest, the growth stage at the application for the 60 DALT is speculated to be between BBCH 79 and 83.

BBCH 83: 30% of pods ripe (beans final colour, dry and hard)

BBCH 85: 50% of pods ripe (beans final colour, dry and hard)

BBCH 86: 60% of pods ripe (beans final colour, dry and hard)

BBCH 87: 70% of pods ripe (beans final colour, dry and hard)

BBCH 89: Full maturity: approx. all pods are ripe; beans final colour, dry and hard (= Harvest maturity)

BBCH 91: About 10% of leaves discoloured or fallen

BBCH 97: Above ground parts of plants dead

FATE OF RESIDUES IN STORAGE AND PROCESSING

In processing

The 2013 Meeting received information on effects of heating in water and processing on imazapic residues in soya bean. The estimated processing factors by the 2013 JMPR are reproduced below.

Table 3 Summary of processing factors for soya bean processing

Processed commodity	N	Processing factor	Mean or best estimate
Meal	3	1.00, 1.00, 1.13	1.04
Defatted meal	1	1.29	1.29
Toasted Meal	1	0.88	0.88
Toasted Defatted Meal	1	1.14	1.14
Oil	2	0.13, 0.14	0.14
Laminated Soya Bean	1	0.71	0.71
Flaked Soya Bean	1	0.50	0.50
Hulls	2	1.00, 1.00	1.00

APPRAISAL

Imazapic is an imidazolinone herbicide for the control of grasses and broadleaf weeds. It was reviewed for the first time by JMPR in 2013 when the residue definition was established for plant and animal commodities to be imazapic for compliance with the MRL and for estimation of dietary intake (The residue is not fat soluble). The Meeting established an ADI of 0–0.7 mg/kg bw and that no ARfD was necessary.

The 2013 JMPR received and considered the plant metabolism study and supervised residue trials on transgenic soya beans; analytical methods, storage stability studies and processing studies on soya beans.

Imazapic was included in the priority list by the CCPR at its Forty-sixth Session in 2014 for evaluation for additional MRLs by this Meeting. The current Meeting received information on the registration of imazapic for application on soya bean cultivars tolerant to imidazolinone herbicides in Brazil. The information on supervised residue trials on imidazolinone-tolerant soya beans provided to the 2013 JMPR is reviewed by the current Meeting against the new GAP in Brazil.

Results of supervised residue trials on crops

The 2013 Meeting received supervised trial data for imazapic on transgenic soya beans. The current Meeting evaluated the data against the new GAP for soya bean cultivars tolerant to imidazolinone herbicides.

Soya bean (dry)

A total of 16 supervised trials were conducted on imidazolinone-tolerant soya beans (transgenic) in different years in Brazil.

The new GAP in Brazil allows a single application of a WG formulation of imazapic (also containing imazapyr) to imidazolinone-tolerant cultivars at the rate of 0.014–0.0175 kg ai/ha (in acid equivalents; for both ground and aerial application) with a PHI of 60 days. For ground applications, the water volume should be 100–200 L/ha and for the aerial application, 40–50 L/ha. The trials employed an application rate of 0.0175 kg ai/ha and the application volume of 200 L/ha.

In one trial in the 2007/2008 growing season, the samples were stored for about 600 days; imazapic was demonstrated to be stable for up to 10 months, the longest storage period tested for imazapic in soya bean. The result of this trial was < 0.01 mg/kg.

Residues arising from the independent supervised residue trials following the critical GAP in Brazil were, in rank order (n=12): < 0.01, < 0.01, < 0.05, < 0.05, 0.05, 0.07, 0.07, 0.10, 0.12, 0.15, 0.23 and 0.25 mg/kg.

The Meeting estimated a maximum residue level of 0.5 mg/kg and an STMR of 0.07 mg/kg.

Fate of residues during processing***Processing***

The 2013 Meeting received information on processing of soya beans. The processing factor for imazapic in soya bean processed products is described below.

Processed commodity	N	Processing factor	Best estimate	STMR-P mg/kg
Soya bean				0.07 (STMR)
Oil	2	0.13, 0.14	0.14	0.01

The residues of imazapic concentrate marginally in defatted meal (processing factor of 1.29), and toasted defatted meal (1.14).

For the purpose of calculating the animal dietary burden, the Meeting calculated median residues for soya bean meal and hulls to be 0.09 mg/kg and 0.07 mg/kg, respectively, using the STMR of soya bean and the processing factors of 1.29 (highest of similar processed commodities) and 1.00, respectively.

Residues in animal products***Estimation of dietary burdens***

The maximum and mean dietary burdens were calculated by the 2013 JMPR using the highest residues or median residues of imazapic estimated at that Meeting on a basis of the OECD Animal Feeding Table. As the highest maximum and mean dietary burden for estimating maximum residue levels and STMRs for foods of bovine origin were calculated on the basis of a ration of 100% grass forage, the inclusion of soya bean feed items, with significantly lower residue levels, would not have any measurable impact on the highest maximum and mean dietary burden.

The addition of soya bean feed items in the calculation of dietary burdens increases by approximately 0.2% the highest maximum and mean dietary burden for poultry. The highest maximum dietary burden calculated at this Meeting (9.65 ppm in feed as compared to 9.63 ppm calculated in 2013) was still lower than the dose of 10.9 ppm in the diet used in the metabolism study in which the TRR in all edible tissues were below the LOQ of 0.01 mg/kg

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed in Annex 1 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 and for estimation of dietary intake): *Imazapic*.

Residue is not fat-soluble.

CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P mg/kg	HR or HR-P mg/kg
		New	Previous		
VD 0541	Soya bean (dry)	0.5		0.07	
OR 0541	Soya bean oil, refined			0.01	

CCN	Commodity	Recommended Maximum residue level (mg/kg)		STMR or STMR-P mg/kg	HR or HR-P mg/kg
		New	Previous		
AB 1265	Soya bean meal			0.09	
AB 0641	Soya bean hulls			0.07	

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) of imazapic were calculated for the 17 GEMS/Food cluster diets using STMRs estimated by the 2013 JMPR and STMR/STMR-P for soya bean and soya bean oil estimated by the current Meeting (see Annex 3 to the 2015 Report). The ADI is 0–0.7 mg/kg bw and the calculated IEDIs were in the same range as those calculated by the 2013 JMPR using the 13 GEMS/Food Cluster Diet (0% of the maximum ADI). The Meeting confirmed its conclusion in 2013 that the long-term intake of residues of imazapic resulting from the uses considered by the current JMPR is unlikely to present a public health concern.

Short-term intake

The 2013 JMPR decided that an ARfD is unnecessary. The current Meeting therefore concluded that the short-term intake of residues of imazapic is unlikely to present a public health concern.

REFERENCES

Doc. ID	Author(s)	Year	Title, Source, published or not
	FAO/WHO	2014	FAO Plant Production and Protection Paper 220, Pesticide Residues in Food 2013, Evaluations 2013 Part I – Residues, Rome, Italy Published
	FAO/WHO	2014	FAO Plant Production and Protection Paper 219, Pesticide Residues in Food 2013, Report 2013, Rome, Italy Published
2007/1065863	Jones B.	2007	Estudo de residuos de Imazapyr e Imazapic em soja cultivance (graos) apos tratamento com BAS 714 01 H em condicoes de campo no Brasil BASF SA, Guaratingueta, Brazil Unpublished
2008/1097470	Resende G., Souza C.	2008	Amendment report 01 RF-1088-06 - Study of residues of Imazapyr and Imazapic in soybean cultivance (grains) after treatment with BAS 714 01 H, under field conditions in Brazil BASF SA, Guaratingueta, Brazil Unpublished
2008/1097471	Resende G.	2008	Amendment report 02 RF-1088-06 - Study of residues of Imazapyr and Imazapic in soybean cultivance (grains) after treatment with BAS 714 01 H, under field conditions in Brazil BASF SA, Guaratingueta, Brazil Unpublished
2010/1010261	Resende G., Marinho E.	2010	Study of residues of Imazapyr and Imazapic in soybean cultivance (grains) after treatment with BAS 714 01 H under field conditions in Brazil for import tolerance BASF SA, Guaratingueta, Brazil Unpublished
2010/1079212	Resende G.	2010	Amendment 01 - Final report 1273-07 - Study of residues of Imazapyr and Imazapic in soybean cultivance (grains) after treatment with BAS 714 01 H under field conditions in Brazil for import tolerance

Doc. ID	Author(s)	Year	Title, Source, published or not
			BASF SA, Guaratingueta, Brazil Unpublished
2010/1127505	Jones B., Takahashi J.	2011	Study of residues of Imazapyr and Imazapic in cultivance soybean (grains) after treatment with BAS 714 01 H under field conditions in Brazil BASF SA, Guaratingueta, Brazil Unpublished
2012/3000423	Jones B., Cardoso B.	2012	Residue study of Imazapyr and Imazapic in GMO soybean grains and aspirated grain fraction (AGF) after treatment with BAS 714 01 H under field conditions in Brazil BASF SA, Guaratingueta, Brazil Unpublished