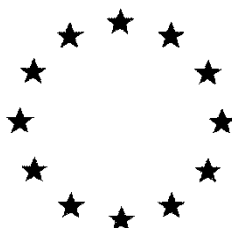


European Commission



**Draft Assessment Report prepared according to the Commission
Regulation (EU) N° 1107/2009**

**Pepino Mosaic Virus, EU strain, mild
isolate Abp1**

**Pepino Mosaic Virus, CH2 strain, mild
isolate Abp2**

Active organism data

**Volume 3 – Annex B.7 Residues in or on treated
products, food and feed**

Rapporteur Member State: Spain

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	Completeness check report of the dossier submitted by the notifier
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B.7 RESIDUES IN OR ON TREATED PRODUCTS, FOOD AND FEED **(ANNEX IIM 6 AND IIIB 8)**

B.7.1 Persistence and likelihood of multiplication in or on crops, feeding stuffs or foodstuffs (Annex IIB 6.3 and Annex IIIB 8)

The preparation AbioProtect® is formulated as a suspension concentrate of tomato plant extract infected with equivalent amounts of PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2.

PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2 are naturally occurring plant viruses (see Documents Vol III MCA sections 1, 3 and 5). Viruses are not able to produce metabolites. PepMV is widespread in Europe; it is present in 19 countries (EPPO, 2017). As PepMV does not always cause visible symptoms in tomatoes (Hanssen et al., 2008), high and chronic exposure of humans towards this virus is expected. Introduction of PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2, in greenhouse (protected) tomato crops is not expected to affect the level of natural occurrence of the virus. Without treatment with AbioProtect®, the crop will most probably be infected with a natural occurring mild or aggressive isolate of the virus.

Therefore, determination of residues of the components of the formulation AbioProtect®, PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2 in or on treated products, food and feed is not considered relevant.

B.7.2 Exposure to consumers (Annex IIB 6.2 and Annex IIIB 8))

B.7.2.1 Non-viable residues

Viruses have no metabolism of their own and are therefore not able to produce secondary metabolites. Because of this reason, there is no risk to consumers and determination and quantification of the residues and metabolites is considered not relevant.

The preparation AbioProtect® is formulated as a suspension concentrate of tomato plants extract infected with equivalent amounts of Pepino mosaic virus (PepMV), EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2. The formulation does not contain any other non-active substances. Other inert ingredients are tomato plant extract and water.

Nicotine (Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)-) has been reported to be present in plants of the Solanaceae family, including tomato (Sheen 1988, Siegmund et al. 1999). Sheen (1988) reported nicotine content of 2.31 ppm in tomato fruits, 2.82 ppm in tomato leaves and 2.77 ppm in tomato stem. However the author indicates that as the determinations were done in a moisture free basis, nicotine content in a fresh weight basis will only be a fraction of 1 ppm. He also suggested that the nicotine presence in tomato might have a biosynthetic origin.

More recently (Siegmund et al. 1999) analysed the presence of nicotine in different products of plants from the Solanaceae family, reporting a content of 2-4 µg/kg (2-4 x 10⁻³ ppm) in fresh tomato fruits. These authors calculated the dietary nicotine intake due to the consumption of potatoes, fresh tomatoes, tomato paste, aubergines and tea to be of 1.4 µg/day (of those 0.089 µg/day could be due to the consumption of fresh tomatoes).

Nicotine has not been approved as an active substance in Europe (2009/9/EC: Commission Decision of 8 December 2008). During the examination of this active substance by the Committee, it was concluded that the existing evidence is not sufficient to demonstrate a safe use with respect to operators, workers, bystanders and consumers (SANCO/2686/08 – rev. 0, 8 August 2008).

The toxicological profile of nicotine was assessed by EFSA in the framework of a previous request regarding nicotine residues in mushrooms in 2009 (EFSA Journal (2009) RN-286, 1-47). EFSA established an acute reference dose (ARfD) of 0.0008 mg/kg body weight (b.w.), based on a lowest observed adverse effect level (LOAEL) of 0.0035 mg/kg b.w. for pharmacological effects after intravenous application of nicotine, using an overall uncertainty factor of 10 and a correction factor of 0.44 for oral bioavailability of nicotine (extrapolation from the intravenous route to the oral route). Due to the short biological half-life of nicotine in humans, it does not accumulate in the body and the most sensitive effect of nicotine is considered to be its pharmacological effect on the cardiovascular system. Therefore, avoiding acute effects of nicotine would also protect from its chronic effects and EFSA established an acceptable daily intake (ADI) for nicotine at 0.0008 mg/kg b.w. per day that is at the same level as the ARfD.

RMS considers that if tomato plant extract is in the formulation, the product may contain nicotine as impurity and it should be considered. No reference to nicotine has been done by the applicant in this section. Data of nicotine content in AbioProtect® has been extracted by the RMS from Section Toxicological and Metabolism studies.

Considering all the information indicated above, the use of AbioProtect® and its components (PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2), as a plant protection product in a single application on the seedlings (BBCH 13-15) is not expected to affect the level of natural occurrence of nicotine in tomato fruits nor the level of exposure of humans to nicotine. Nonetheless, the nicotine content in PepMV, EU strain, mild isolate Abp1 and in PepMV, CH2 strain, mild isolate Abp2 has been determined.

Nicotine content in five independent batches of PepMV, EU strain, mild isolate Abp1 and of PepMV, CH2 strain, mild isolate Abp2 has been determined by a validated analysis method with a quantification limit of 0.003 mg/kg by an external independent laboratory as reported in Vol 4. The results show that there is very low content of nicotine in the active substances (PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2), as AbioProtect® is a suspension concentrate (SC) formulated with equivalent amounts of each of the active substances, it has a very low content of nicotine.

The maximum nicotine content in the five batches of PepMV, EU strain, mild isolate Abp1 analysed was 0.102 mg/L with a medium content of 0.027 mg/L. While the maximum nicotine content in the five batches of PepMV, CH2 strain, mild isolate Abp2 analysed is 0.111 mg/L, with a medium content of 0.05 mg/L. AbioProtect® is formulated with equivalent amounts of PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2, the maximum application rate is 1.6 L of AbioProtect®, which leads to a maximum of 0.1704 mg of nicotine /ha, in the worst possible scenario. Therefore an exposure assessment is conducted based on this data.

Although the active substance, or the nicotine content in the tomato leaves used to produce them, are not expected to pose a threat, an exposure assessment is required for the nicotine that might be present in AbioProtect®. Therefore, an estimation of potential exposure to the metabolite nicotine has been carried out by the RMS, since it was not submitted by the applicant.

According to the FAOstat data from year 2016 yield in the EU countries varies between 8686 kg/ha in Latvia and 507042 kg/ha in the Netherlands. Considering a worst case with yield data of 8686 kg/ha and assuming that all residue will systemically transfer to the growing tomato fruits and not to other plant parts (thus considering nicotine to be systemic and not degradable), residue at harvest would be 0.00002 mg nicotine per kg tomatoes.

Acute and chronic exposure to nicotine for adults, children and general populations has been estimated using the model created by EFSA including all available EU Member State diets: PRIMo (Pesticide Residue Intake Model rev. 2). The result of the chronic exposure assessment was below the ADI with a Theoretical Maximum Daily Intake (TMDI) of 0.01% for WHO cluster diet B.

The estimated short-term intake for deltamethrin residues expected in tomato accounted for 0.1% of the ARfD.

The levels of nicotine in the formulation AbioProtect® do not represent unacceptable acute and chronic risks for the consumer.

B.7.2.2 Viable residues

The preparation AbioProtect® is formulated as a suspension concentrate of tomato plant extract infected with equivalent amounts of PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2, which are naturally occurring plant viruses (see Documents M-MA Sections 1, 3 and 5). As viruses like PepMV are ubiquitous in plants and fruits, human exposure to the virus is likely to be high. There are no documented cases of plant viruses causing diseases in humans. Moreover, no acute toxicity, mutagenicity or infectiveness was observed in the acute toxicity, mutagenicity and infectiveness studies. Therefore, determination of residues of AbioProtect® components, PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2 in or on treated products, food and feed is not considered relevant.

B.7.3 Summary and evaluation of residue behaviour (Annex IIM6.5 and Annex IIIB 8))

Plant viruses like PepMV are ubiquitous in plants and fruits, and as a consequence they are continuously consumed by people. Cases of plant viruses causing diseases in humans have never been documented and none of them so far is known as pathogen to animals and human beings.

Viruses have no metabolism of their own and are therefore not able to produce secondary metabolites.

The studies provided in the toxicology dossier demonstrate that the plant protection product AbioProtect® and its components PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2 are neither toxic nor pathogenic for rats. Furthermore these studies have also shown that the formulation and its components do not affect cell viability and cell proliferation of human epithelial cell type 2 A549, and do not infect or replicate in this human cell line.

Therefore, it could be concluded that the establishment of an MRL is not required for AbioProtect® and its components PepMV, EU strain, mild isolate Abp1 and PepMV, CH2 strain, mild isolate Abp2.

B.7.4 References

A document has been submitted by the applicant with the summaries and results of the scientific peer-review open literature, on the active substance and its relevant metabolites dealing with side-effects on health, the environment and non-target species and published within the last 10 years before the date of submission of the dossier, extracted from the information accessible to the general public. However a description of how this process of search, selection and reviewing has been carried out has not been submitted by the applicant. Therefore RMS cannot confirm that open literature fulfill the requirements of the EFSA Guidance “Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009”.

Andersson, C., Weenström, P., Gry, J., 2003. Nicotine alkaloids in Solanaceous food plants,

TemaNord 2003:531

EFSA (European Food Safety Authority), 2009. Potential risks for public health due to the presence of nicotine in wild mushrooms. EFSA Journal (2009) RN-286, 1-47 Parma, Italy,

Hanssen I.M., Paeleman A., Wittemans L., Goen K., Lievens B., Bragard C., Vanachter A., Thomma B. (2008) Genetic characterization of Pepino mosaic virus isolates from Belgian greenhouse tomatoes reveals genetic recombination. European Journal of Plant Pathology 121. DOI: 10.1007/s10658-007-9255-0.

Siegmund B., Leitner E. and, and Pfannhauser W. (1999) Determination of the Nicotine Content of Various Edible Nightshades (Solanaceae) and Their Products and Estimation of the Associated Dietary Nicotine Intake. Journal of Agricultural and Food Chemistry, 47 (8), 3113-3120. doi: 10.1021/jf990089w.

Sheen SJ (1988). Detection of nicotine in foods and plant materials. Journal of Food Science, 53 (5) 1572-1573.

The literature search provided was conducted in accordance to the guidelines set up in document European Food Safety Authority; Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (OJ L 309, 24.11.2009, p.1-50), (EFSA Journal 2011; 9(2):2092. [49pp.]. doi:10.2903/j.efsa.2011.2092). Full details and justification of how the literature search was performed could be found in Document K-MA 5.2.5 Hernando 2017.

Appendix 1A EFSA PRIMo, model for chronic and acute risk assessment - rev. 2_0 (residue of nicotine)

		nicotina				Prepare workbook for refined calculations	
		Status of the active substance: not included		Code no.			
		LOQ (mg/kg bw):		proposed LOQ:			
		Toxicological end points					
		ADI (mg/kg bw/day): 0,0008		ARID (mg/kg bw): 0,0008		Undo refined calculations	
		Source of ADI: EFSA 2009		Source of ARID: EFSA 2009			
		Year of evaluation:		Year of evaluation:			
Chronic risk assessment							
TMDI (range) in % of ADI minimum - maximum							
No of diets exceeding ADI: ---							
	Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)
	0,01	WHO Cluster diet B	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	IT kids/toddler	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	IT adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	WHO regional European diet	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	WHO cluster diet D	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	ES child	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	DE child	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	PT General population	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	PL general population	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	ES adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	FR toddler	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	SE general population 90th percentile	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	WHO Cluster diet F	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	NL child	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	UK vegetarian	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	LT adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	UK Toddler	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	DK child	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	WHO cluster diet E	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	UK Adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	FR all population	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	NL general	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	FI adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	DK adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	IE adult	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	UK Infant	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
	0,0	FR infant	0,0	Tomatoes		FRUIT (FRESH OR FROZEN)	FRUIT (FRESH OR FROZEN)
Conclusion:							
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.							
A long-term intake of residues of nicotina is unlikely to present a public health concern.							

