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LENACIL

Volume 3 – B.3 (AS)

Rapporteur Member State : Belgium
Co-Rapporteur Member State : Austria

Version History

When	What
November 2007 – July 2009	Draft Assessment Report (DAR) – prepared by RMS BE in the context of the inclusion of the a.s. in Annex I to Council Directive 91/414/EEC. Updated versions of the initial DAR, as well as addenda to the initial DAR, were issued in the period February 2009 – May 2009 (before and after experts' meetings) and were compiled by EFSA in a final 'addendum' dated July 2009.
December 2012 – March 2013	Addenda to DAR Vol.3, B.8 and B.7 (Environmental Fate & Behaviour and Residues), respectively – prepared by RMS BE in the context of the evaluation of confirmatory information requested by Commission Directive 2010/39/EU.
May 2016	Update of DAR Vol.3, B.6 (Toxicology and metabolism) – prepared by RMS BE in the context of the evaluation of confirmatory data on the relevance of ground water metabolites (following classification of lenacil according to Reg. (EC) No 1272/2008).
May 2019	Draft Renewal Assessment Report (DRAR) – prepared by RMS BE in the context of the application for renewal of approval of the a.s. according to Reg. (EU) No 844/2012. *Note: The DRAR is a stand-alone document containing the evaluations already displayed in the initial DAR (incl. its addenda and updated versions), as well as the new assessments. The revision of the initial DAR has been done in accordance with SANCO/10180/2013 rev.1 (March 2013), with changes to the original text – resulting from assessment of new studies (or reconsideration of old studies or studies that were not yet previously peer-reviewed) – being highlighted by means of yellow shading.* *Changes to the original conclusions have been highlighted in level 2 of Vol.1.*

The RMS is the author of the Assessment Report. The Assessment Report is based on the validation by the RMS, and the verification during the EFSA peer-review process, of the information submitted by the Applicant in the dossier, including the Applicant's assessments provided in the summary dossier. As a consequence, data and information including assessments and conclusions, validated and verified by the RMS experts, may be taken from the applicant's (summary) dossier and included as such or adapted/modified by the RMS in the Assessment Report. For reasons of efficiency, the Assessment Report should include the information validated/verified by the RMS, without detailing which elements have been taken or modified from the Applicant's assessment. As the Applicant's summary dossier is published, the experts, interested parties, and the public may compare both documents for getting details on which elements of the Applicant's dossier have been validated/verified and which ones have been modified by the RMS.

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B.3. DATA ON APPLICATION

Unless specifically indicated, all reports in this section are submitted to address mandatory data requirements for the approval of active substance.

B.3.1. USE OF THE ACTIVE SUBSTANCE

Plant protection products containing lenacil are to be used for control of annual dicotyledonous weeds (3ANDIT) in sugar and fodder beets (BEAVA, BEAVC). Application may be performed between the first visible leaf stage of the crop (BBCH 10) and until leaves cover 10% of the ground (BBCH 31).

The good agricultural practice in sugar and fodder beets recommends the use of lenacil as part of the Repeated Low Dose Program (RLDP)[1] which consists in the application of a tank mix of several herbicides with different modes of action at a rate which is adapted to the development stage of each weed flush. Within this program, the number of applications has an influence on efficacy because each application is made on very small weeds and the practical interest of lenacil is its residual effect.

B.3.2. FUNCTION

Lenacil is a post-emergence herbicide for the control of various species of annual dicotyledonous weeds (3ANDIT) to protect sugar and fodder beets (BEAVA, BEAVC). Its absorption by the plant is primarily done by the roots, but can also be foliar. Lenacil is systemic, it migrates towards its sites of action. It inhibits the photosynthesis and adventitious leaves are turning yellow and die.

B.3.3. EFFECTS ON HARMFUL ORGANISMS

Lenacil is an herbicide that belongs to the substituted uracil chemical family. Uracils are potent direct inhibitors of photosynthesis activity at chloroplast level. They block the Hill reaction and interfere with a step in the photosynthetic pathway close to oxygen evolution. First symptoms of effect show a discoloration of the leaf veins followed by chlorosis, necrosis and eventual death of plants.

Absorption of lenacil by the plant mainly occurs via the root system, but can also be foliar. Lenacil is systemic, it migrates towards its sites of action (translocation occurs primarily via the xylem, from roots to leaves). It inhibits the photosynthesis and adventitious leaves are turning yellow and die. Weeds should not have developed more than two leaves at application date. Best control is achieved when the soil is humid and there are fine crumbles but no clumps and/or plant remains. Rain favours the transport of lenacil in the roots. If conditions are dry for a long period of time after application weed control might be unsatisfactory.

B.3.4. FIELD OF USE ENVISAGED

Lenacil is to be used in agriculture under field conditions only.

B.3.5. HARMFUL ORGANISMS CONTROLLED AND CROPS OR PRODUCTS PROTECTED OR TREATED

Lenacil is an herbicide for the control of various species of annual dicotyledonous weeds (3ANDIT) to protect sugar and fodder beets (BEAVA, BEAVC). Weeds considered susceptible or very susceptible to lenacil in the Central and/or the South Zone (on the basis of informative data from See Volume 3 CP B3) are *Amaranthus retroflexus* (AMARE), *Brassica napus* (BRSNN), *Capsella bursa-pastoris* (CAPBP), *Fumaria officinalis* (FUMOF), *Galium aparine* (GALAP), *Lamium purpureum* (LAMPU) *Matricaria chamomilla* (MATCH), *Myosotis arvensis* (MYOAR), *Polygonum aviculare* (POLAV), *Fallopia convolvulus* (POLCO), *Sinapis arvensis* (SINAR), *Stellaria media* (STEME), *Thlaspi arvense* (THLAR), *Veronica persica* (VERPE) and *Viola arvensis* (VIOAR).

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[1] Publicly available literature of decades of sugar beet research can be found in several Member States. Sugar beet research Institutes of EU (e.g., IFZ in DE, IRBAB/KBIVB in BE, ITB in FR, IRS in NL), but also DANISCO, British Sugar, SÜDZUCKER and AGRANA are members of the IIRB (International Institute for Beet Research).

B.3.6. MODE OF ACTION

Lenacil is an herbicide that belongs to the substituted uracil chemical family. Uracils are classified under HRAC group C1, inhibitors of photosynthesis at photosystem II. Lenacil is a photosynthesis inhibitor working on Photosynthetic Electron Transport (PET) mechanisms. Uracils are potent direct inhibitors of photosynthesis activity at chloroplast level. They block the Hill reaction and interfere with a step in the photosynthetic pathway close to oxygen evolution.

Lenacil inhibits photosynthesis by binding to the QB-binding niche on the D1 protein of the photosystem II complex in the thylakoid membranes of the chloroplast. This binding blocks electron transport from QA to QB and thus stops CO_2 fixation and production of the ATP and NADPH2 needed for plant growth, usually plant die from other processes. The inability to re-oxidize QA promotes the formation of triplet state chlorophyll which interacts with ground state oxygen to form singlet oxygen. Singlet oxygen attacks lipids and proteins resulting in loss of chlorophyll and carotenoids and disintegration of membranes. Both triplet chlorophyll and singlet oxygen can initiate a chain reaction of lipid peroxidation.

Its absorption by the plant is primarily done by the roots, but can also be foliar. It has a systemic action and migrates towards its sites of action. It inhibits the photosynthesis and adventitious leaves are turning yellow and die. Weeds should not have developed more than two leaves at application date. Best control is achieved when the soil is humid and there a fine crumbles but no clumps and/or plant remains. Rain favours the transport of lenacil in the roots. If it is dry for a long period of time after application weed control might be unsatisfactory.

B.3.7. INFORMATION ON THE OCCURRENCE OR POSSIBLE OCCURRENCE OF THE DEVELOPMENT OF RESISTANCE AND APPROPRIATE MANAGEMENT STRATEGIES

This point reviews the resistance risk analysis, and sets out management strategies for products that contain lenacil, based on Guideline 7600/VI/95 rev. 6 and EPPO Guideline 213 rev. 4. Detailed consideration will occur in the subsequent product authorisation process and will include information on other active substances that might be co-formulated with lenacil as well as more detailed data related to biology of target weed (that are relevant for specific products) in relation to resistance and data on national resistance situations. The resistance situation described here under reflects cases listed on www.weedscience.org as of October 2018.

Chemistry

Lenacil is an herbicide that belongs to the substituted uracil chemical family. Uracils are classified under HRAC group C1, inhibitors of photosynthesis at photosystem II. Inhibitors of photosynthesis at photosystem II include subclasses C1, C2 and C3 that display different binding behaviours at the binding protein D1. They also encompass phenyl-carbamates, pyridazinones, triazines, triazinones, triazolinone (HRAC group C1), amides, ureas (HRAC group C2), benzothiadiazinones, nitriles and phenyl-pyridazines (HRAC group C3).

Photosynthesis involves biophysical capture and transduction of sunlight energy to drive electron transport to produce NADPH and ATP for the carbon reduction cycle. Many herbicides across several structurally diverse chemical groups (see here above) inhibit photosynthesis through the same mechanism of action. They compete with plastoquinone (PQ) at the PQ binding site on the D1 protein within the photosystem two (PSII) complex. PSII electron transport inhibition stops NADPH and ATP production and the carbon reduction cycle, leading to carbohydrate starvation and oxidative stress.

The basis for the vast majority of the weed biotypes with resistance to PSII inhibitor herbicides is a point mutation in the maternally inherited chloroplastic psbA gene encoding the D1 protein causes a Ser-264-Gly amino acid substitution in the PQ binding site.

Since Ryan[2] (1970) first publication occurred, resistance to inhibitor of PSII photosystem has globally evolved in 74 weed species (51 dicotyledons and 23 monocotyledons) worldwide. In Europe six cases of resistance to the Uracil chemical family, in particular to lenacil, has been reported, five from Czech Republic and one in Belgium. Cases in Czech Republic were the following: In 1982 on *Polygonum lapathifolium* with resistance reported to atrazine, cyanazine, lenacil, prometryn, terbuthylazine and terbutryne on railway. In 1986 on *Chenopodium album*

[2] Ryan GF. 1970. Resistance of common groundsel to simazine and atrazine. *Weed Sci.* 18:614–16

with resistance reported to atrazine, cyanazine, lenacil, prometon, simazine, terbuthylazine and terbutryne in corn and sugarbeet. In 1988 on *Senecio vulgaris* with resistance reported to atrazine, cyanazine, lenacil, prometryn, simazine, terbuthylazine and terbutryne in orchards and on railways. In 1989 on *Polygonum persicaria* and *Chenopodium strictum* with resistance reported to atrazine, cyanazine, lenacil, prometryn, simazine, and terbutryne on railways, in corn and sugarbeet. The case in Belgium was the following: In 2015 on *Atriplex patula* with resistance reported to desmedipham, lenacil, metamitron, and phenmedipham in sugarbeet.

Cases of cross resistances within photosynthesis inhibitors at photosystem II have been observed. The risk resulting from the mode of action of the active substance (chemistry) is considered to be moderate to high.

Biology

Among weeds considered susceptible or very susceptible to lenacil (B.3.5), some species are concerned by a lot of cases of resistances (to herbicides of various modes of action), such as *Amaranthus retroflexus* (AMARE) with 47 cases and *Stellaria media* (STEME) with 23 cases. The risk resulting from the target weeds of lenacil (biology) is considered to be high.

Inherent risk of resistance

The inherent resistance risk is a combination of both the risk resulting from the target weeds (i.e. the biology) and the risk resulting from the mode of action of the active substance (i.e. the chemistry). Among resistance cases for *Amaranthus retroflexus* (AMARE), most of them concern inhibitors of photosynthesis at photosystem II. The inherent unrestricted use of lenacil leads to an unacceptable risk of resistance weeds development. Resistance management is therefore necessary.

Resistance management

The notifier will continue to promote the resistance management plan on product literature and during technical sales training meetings with customers and growers. Guidelines are given as the source of additional information pertinent to the grower and/or adviser. They are designed to delay or prevent resistant weeds from becoming a problem.

These guidelines include the use of a suitable product with an alternative mode of action either in sequence or in tank-mixture with the product that contains lenacil. Preferably, these should be short soil-residual herbicides in order to prevent the development of metabolic resistance resulting from long-term exposure of weeds. Tank mixes and sequential treatments are already commonly used for sugar beet herbicides. As a result, the eventuality of the spreading of a resistant individual in a sugar beet field is usually very low. Guidelines also involve the use of crop rotations. Sugar beet, the target crop for lenacil use, is nearly always rotated with other crops such as wheat, barley, and oilseed rape. Monocultures of sugar beet are extremely rare. The use of tillage in conjunction with herbicides is also recommended where practical. The best herbicide resistant weed management program uses a balanced variety of control methods, including herbicides with different modes of action and conventional soil tillage.

An example of label including some of these guidelines as well as a broad explanation regarding resistance and reference to the resistance action group is mentioned hereafter:

When herbicides with the same mode of action are used repeatedly over several years in the same field, selection of resistant biotypes can take place. These can propagate and may become dominating. A weed species is considered resistant to an herbicide if it survives a correctly applied treatment at the recommended dose. Development of resistance within a weed species can be avoided or delayed by alternating (or tank mixing) with suitable products having different mode of action.

Cultural practices (ex: ploughing, late sowing,…) are also effective tools to be used in conjunction with chemical tools in preventing resistance. A strategy for preventing and managing resistance should be adopted. The Weed Resistance Action Groups have produced guidelines and copies are available from the HGCA, BAA, etc. your distributor, crop adviser or product manufacturer.

The monitoring strategies employed will also be based on the investigation of complaints from growers of apparent loss of field performance. Providing that all other aspects negatively impacting field performance can be ruled out, samples will be taken and tested for resistance. The notifier will undertake to inform the appropriate authority of any confirmed resistant cases arising directly from the use of products that contain lenacil.

Conclusion
When applying the modifiers (resistance management) proposed by the applicant, the risk is reduced and the use of lenacil can be considered as presenting a low risk of resistance. The proposed modifiers are part of the good agricultural practice and can be easily applied by end-users. Moreover, the good agricultural practice in sugar beet recommends the application of the Repeated Low Dose Program (RLDP) which consists in the application of a tank mix of several herbicides with different modes of action at a rate which is adapted to the development stage of each weed flush. This system is by itself a good resistance management strategy. On top of resistance management proposed by the applicant here above, promotion of the use of a RLDP is necessary.

B.3.8. REFERENCES RELIED ON

Document M-CA, section 3

www.weedscience.org

Ryan GF. 1970. Resistance of common groundsel to simazine and atrazine. Weed Sci. 18:614–16

Publicly available literature of decades of sugar beet research can be found in several Member States. Sugar beet research Institutes of EU (e.g., IFZ in DE, IRBAB/KBIVB in BE, ITB in FR, IRS in NL), but also DANISCO, British Sugar, SÜDZUCKER and AGRANA are members of the IIRB (International Institute for Beet Research).