Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009** as it applies in Great Britain (GB PPP)

Cinmethylin (BAS 684 H)

Volume 3 – B.3 (AS)
Data on application

Great Britain

November 2020

Version History

When	What
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B.3. DATA ON APPLICATION

B.3.1. USE OF THE ACTIVE SUBSTANCE

Cinmethylin is a soil residual herbicide under development for the control of important annual grass weed species and broadleaf weeds in arable crops. BASF have included winter wheat and winter barley in their proposed GAP table for Great Britain. BASF have also included winter oilseed rape in their proposed GAP table of representative uses. However, this has not been included as an intended use in Great Britain. No data have been submitted to support use in winter oilseed rape. However, under Regulation 1107 Annex II point 3.2 it is stated that "an active substance alone or associated with a safener or synergist shall only be approved where it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective". BASF have demonstrated efficacy and crop safety of the representative use on winter wheat. The proposed use on oilseed rape falls within that of the proposed uses on winter cereals. This is sufficient to meet the requirements set with Regulation 1107. However, the individual claims and any future uses will all be assessed in detail at product authorisation stage.

This is in line with the principles established in SANCO/10054/2013 - rev. 3'Guidance Document on Data Requirements on Efficacy for the Dossier to be Submitted for the Approval of New Active Substances Contained in Plant Protection Products' where the 'principal objective of the efficacy evaluation of an active
substance is to confirm that the doses are realistic for the GAP submitted for risk evaluation and approval and representative for all subsequent authorisations.'

The proposed uses are as follows:

Crop and/or situation (a)	**Region**	**Product Name**	**Pests or group of pests controlled (c)**	**Formulation**		**Application**			**Application rate per treatment**			**Remarks (m)**
				Type (d-f)	Rate L/ha	Method kind (f-h)	Growth stage and season (j)	Number min max (k)	Kg a.i./ha min max (g/hl)	Water l/ha min max	Lk a.i./ha min max (*) (g/ha)	
winter wheat (TRZAW), winter barley (HORVW)	**GB**	BAS 684 03 H	blackgrass (ALOMY), ryegrass (LOLSS),	-	0.666	SP	pre-emergence (BBCH 00-08)	a) 1 b) 1	a) 0.500 b) 0.500	100 - 400	-	Representative use
winter wheat (TRZAW), winter barley (HORVW)	**GB**	BAS 684 03 H	blackgrass (ALOMY), ryegrass (LOLSS),	-	0.666	SP	post-emergence (BBCH 09-29	a) 1 b) 1	a) 0.500 b) 0.500	100 – 400	-	Representative use
winter wheat (TRZAW), winter barley (HORVW)	**GB**	BAS 684 03 H	annual meadowgrass (POAAN) and annual dicots	-	0.666	SP	pre-emergence (BBCH 00-08)	a) 1 b) 1	a) 0.250 b) 0.250	100 – 400	-	Representative use
winter wheat (TRZAW), winter barley (HORVW)	**GB**	BAS 684 03 H	annual meadowgrass (POAAN) and annual dicots	-	0.666	SP	post-emergence (BBCH 09-29)	a) 1 b) 1	a) 0.250 b) 0.250	100 - 400	-	Representative use

B.3.2. FUNCTION

Cinmethylin is used as an herbicide for the control of important annual grass weed species and broadleaf weeds at a dose of 0.25 kg a.s/ha.

B.3.3. EFFECTS ON HARMFUL ORGANISMS

Cinmethylin is providing soil residual and foliar activity with application either before or after weed emergence, leading to root and shoot growth inhibition of sensitive plants. After uptake cinmethylin is translocated acropetally within the xylem.

After green leaf area starts to show symptoms of discoloration and yellowing, affected plants wither and die back due to starvation of the plant, as absorbed sunlight can no longer be transformed into energy to sustain plant viability.

B.3.4. FIELD OF USE ENVISAGED

Agriculture.

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

Cinmethylin, formulated as a 750 g/l EC-formulation have been tested widely on a range of annual grasses and broadleaf weeds important in winter wheat and oilseed rape. The specific weed control claims will be considered in subsequent product authorisations. The following target weeds have been identified:

Table .3.5-1: Target weeds of BAS 684 H

Crop	Target Weed	Dose rate g a.s./ha
Winter wheat	*Alopecurus myosuroides*	500
	Lolium spp.	500
	Apera spica-venti	250
	Poa annua	250
	Papaver rhoeas	250
Winter oilseed rape	*Apera spica-venti*	250
	Poa annua	250
	Papaver rhoeas	250

Efficacy evaluation for the use in oilseed rape will be addressed with the individual biological assessment dossiers for the corresponding future product authorisations.

B.3.6. MODE OF ACTION

Cinmethylin inhibits a unique and novel target enzyme in fatty acid (FA) biosynthesis for which no HRAC-classification have been assigned yet. FAs and FA-derived complex lipids are essential in living organisms. They are important components of cellular membranes and signalling molecules, and they serve as a major energy reserve in storage tissues. Therefore, depleting plants of FAs has dramatic physiological impact. Cell membranes are irreversibly disrupted, which has a detrimental effect on emerging plant tissue. In pre-emergence treatments, seedlings quickly become non-viable when FA storage is exhausted. In addition, transport and receptor functions, indispensable for photosynthetic activity can no longer be fulfilled. This results in starvation of the plant, since absorbed sunlight can no longer be transformed into energy to sustain plant viability.

In plant cells, early FA biosynthesis is carried out in the plastids. Intermediate FAs with chain lengths of 16 or 18 carbon atoms bind to an acyl carrier protein (ACP) prior to export into the cytosol and further downstream processing. Before they can be exported, however, their chain elongation process must be terminated. This termination is carried out by an enzyme family called fatty acid thioesterase (FAT), which releases the FA from its acyl carrier protein. Cinmethylin uniquely targets the FAT enzyme family located in the plastid to prevent the termination process. Other known chemical classes (DIMs/FOPs) also inhibit fatty acid biosynthesis in the plastids. However, the enzyme target is acetyl-CoA carboxylase (ACCase), which is the first step in fatty acid biosynthesis and a distinctly different target site to FAT. In contrast, VLCFA inhibitors, which also affect lipid biosynthesis, exert their inhibition in the endoplasmic reticulum, which is a distinctly different compartment in the plant cell.

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

A detailed consideration of the resistance situation was presented in Section Doc M-CA Section 3.7 and the Biological Assessment Document (BAD) for the associated product assessment for BAS 684 03 H. This has been summarised below.

Mechanism of Resistance

Principally, resistance to herbicides can be caused by target site modification or mechanisms not related to the target site, of which increased herbicide metabolism plays a major role.

An altered target site within a plant may mean that an herbicide no longer binds to its normal site of action due to a change in the structure of the target site, thereby allowing the plant to survive the herbicide treatment which relies on this site for its activity. This usually results in complete resistance to herbicides acting on that specific site but not to herbicides acting on different targets.

Non-target site resistance, e.g. enhanced metabolism is often not specific to a certain mode of action. The level of response to these mechanisms can greatly differ between products of the same chemistry or could affect in parallel products of different mode of action.
Enhanced metabolism means that the resistant plant can degrade a herbicide to non-phytotoxic substances faster than a normal sensitive plant, thereby surviving a herbicide treatment in much the same manner as many crop plants.
The impact of this resistance mechanism on the performance of individual herbicides is highly variable and tends to gradually increase over time.
Different mechanisms could occur in the same plant expressing resistance to one or several herbicidal active components.

Evidence of Resistance, Cross-Resistance and Sensitivity Testing

BAS 684 H is a new active substance to Europe and as such has never been used in Europe before. Furthermore, the novel Mode of Action of BAS 684 H is not related to any other herbicide class used by farmers for the control of grasses and broadleaf weeds. Therefore, no selection pressure has been ever exerted by this mode of action and no target-site cross-resistance to other herbicides currently exists.

Sensitivity testing on numerous *Alopecurus myosuroides* accessions from important cereal and oilseed growing regions across different countries in Europe was conducted in the greenhouse to investigate potential cross-resistance patterns. Results were as follows;

- 77 biotypes out of a total tested 196 accessions were classified as being resistant (RR, RRR) to 'Atlantis WG' (mesosulfuron-methyl + iodosulfuron-methyl-sodium). At 25% of the targeted field dose rate, BAS 684 H provided excellent activity on these accessions, irrespective of their R-classification for Atlantis WG. Even though the impact of non-target site mechanisms on the 'Atlantis WG' resistance cannot be quantified, the low to moderate frequency level of the most important mutations at loci Pro197 and Trp574 suggest that the non-target-site mechanisms present in the tested biotypes do not confer cross-resistance to BAS 684 H.
- Baseline sensitivity testing on 21 accessions identified in general a higher variation in susceptibility between accessions but also across individual trials carried out. BAS 684 H provided ≥80% control at 25 % of the targeted dose rate, except for one accession which varied in the required dose rate between 25-50% of the field dose in different trials.
- Visual susceptibility assessments followed by an R-classification according to S. Moss were conducted on 288 accessions. At 25% of the BAS 684 H targeted dose rate, 17 accessions did show a slight decline in control level, while for the reference product the 25% dose rate indicated a slight control reduction already on 52 accessions with additional 25 / 1 accessions grouped into the resistance classes RR or RRR.

Overall it can be concluded that *Alopecurus* shows a smaller variation in the susceptibility to BAS 684 H than to the standard reference and that no incidences of biotypes resistant to BAS 684 H have currently been observed.

Additionally, in field trials performed by BASF in Europe, no herbicide-resistant weeds to BAS 684 H were identified.

Resistance risk conclusion

Cinmethylin is a new herbicide in the GB and wider EU and represents a novel mode of action. However, the active substance has been authorised for some years in Australia and Asia. Currently no cases of resistance have been recorded according to the International Survey of Herbicide Resistant Weeds (www.weedscience.org). The data presented in the baseline sensitivity trials above do not demonstrate any significant indication of reduced activity in the biotypes tested. Therefore, HSE considers that the resistance risk of the active substance itself is low. However, the targets proposed include the major grassweed Blackgrass. Blackgrass is major agricultural weed of cereals with an extensive history of resistance issues. As such the inherent risk of this target is considered to be high. Therefore, HSE considers that the overall inherent risk of resistance developing to cinmethylin is moderate rather than low as proposed by the applicant. Therefore, resistance management strategies will need to be considered.

The applicant has proposed the following resistance management strategy:

- Always follow HRAC guidelines for preventing and managing herbicide resistant weeds.
- Maximize the use of cultural control measures wherever possible (e.g. crop rotation, ploughing, stale seedbeds, delayed drilling, etc).
- Adopt as diverse a rotation as possible using autumn and spring sown crops.
- Use a program of tank mixes or herbicide sequences with different modes of action within individual crops or succeeding crops. Do not rely on one herbicide mode of action for the control of grass or broad-leaved weeds in the same field over several years.
- Apply post-emergence products/mixtures to small, actively growing weeds to maximize the level of control.
- Scout fields regularly and investigate the reasons for any poor control.

HSE considers that the resistance management strategy proposed is acceptable. Due to this high-risk nature of the target weed Blackgrass HSE considers a monitoring strategy is required at product authorisation.

Cinmethylin; racemic mixture

Cinmethylin is a racemic mixture, consisting therefore of a 50:50 ratio of the plus-enantiomer and the minus-enantiomer.

The efficacy of the individual isomers was investigated in a 2018 trial (see KCA_3.2/001). In a greenhouse trial both the R (-) and S (+) enantiomers were tested against the weed species *Apera spica-venti* (APESV) and *Poa annua* (POAAN). In this trial the R (-) enantiomer showed a similar activity as BAS 684 H while the S (+) enantiomer was slightly less efficacious. However, the two enantiomers both have indicated a good biological activity against weed species tested.

On the basis of these data it is concluded that both isomers have efficacy activity.

B.3.8. REFERENCES RELIED ON

Data Point	Author (s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
Volume 3 CA point B.3.	Mayer, F	2018	Further information on the active substance	N			Company	None.
KCA 3.2/1	Kraemer, G	2018	Herbicidal efficacy of BAS 684 H enantiomers (Reg.No. LS5925581 and LS5925632) 2018/1069982	N			Company	None.
KCA 3.7/1	Sievernich, B	2018	a Resistance risk analysis for BAS 684 H in Europe 2018/1050814	N			Company	None.