Peer review of the pesticide risk assessment for the active substance bromoxynil in light of negligible exposure data submitted

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Abstract

The conclusions of EFSA following the peer review of the initial risk assessment carried out by the competent authority of the rapporteur Member State France for the pesticide active substance bromoxynil are reported. The European Commission requested EFSA to conduct a peer review and provide its conclusions on whether exposure of humans to bromoxynil can be considered negligible, taking into account the European Commission’s draft guidance on this topic. The conclusions were reached on the basis of the evaluation of the representative uses of bromoxynil as a herbicide on maize and straw cereals. The reliable endpoints, derived from the studies and the literature data presented in the dossier and considered appropriate for use in regulatory risk assessment, are presented.

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Keywords: bromoxynil, peer review, negligible exposure, risk assessment, pesticide, herbicide

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Summary

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as the Regulation’) lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Bromoxynil is one of the active substances listed in Regulation (EU) No 686/2012. The European Food Safety Authority (EFSA) finalised a conclusion on the peer review of the pesticide risk assessment of the active substance bromoxynil according to Article 13 of Regulation (EU) No 844/2012 on 14 June 2017 and provided its conclusion to the European Commission.

In 2017, during the peer review for the renewal of approval, EFSA proposed to classify bromoxynil (and its esters) as toxic for reproduction category 1B, leading to a critical area of concern with regard to the approval criteria of Annex II, Point 3.6.4. of Regulation (EC) No 1107/2009. In addition, bromoxynil and its esters are currently classified as toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and toxic effects on the endocrine organs were observed in the data available during the peer review. Therefore, the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine-disrupting properties may be met.

Given the proposal for classification made during the peer review and the potential impact on the renewal of the approval, the European Commission invited the applicant Bayer CropScience, on behalf of the Bromoxynil Task Force to provide further information to demonstrate that the exposure of humans to bromoxynil is negligible under realistic conditions of use.

The European Commission then requested the rapporteur Member State (RMS), France, to carry out an evaluation of this information and to submit its assessment in the format of an addendum to the renewal assessment report (RAR) to EFSA. The applicant, Bayer CropScience, on behalf of the Bromoxynil Task Force submitted an updated dossier in January 2018, which was evaluated by the RMS, France, in the form of a revised RAR. The RMS provided the revised RAR on 26 June 2018 to EFSA. EFSA distributed the addendum to all Member States and applicant for comments on 27 June 2018, and provided comments as well. EFSA collated all comments received and provided its scientific view on these comments received. The addendum and the compiled commenting table were discussed at an expert consultation in the area of toxicology in September 2018. Details of the issues discussed, together with the outcome of these discussions were recorded in the meeting report. A final consultation on the conclusions arising from the peer review took place with Member States via a written procedure in October 2018.

Considering the representative uses on maize, winter cereals (barley, wheat, rye and oats) and spring cereals (barley, wheat, rye and triticale) the short-term dietary exposure was 1.1% of the acute reference dose (ARfD) and the long-term was below 3.8% of the acceptable daily intake (ADI). Residues according to the provisional residue definition for risk assessment as determined in residue trials were below the lowest validated limit of quantification (LOQ) for cereals grain of 0.01 mg/kg while in feed items were up to 0.02 mg/kg. If the currently established maximum residue levels (MRLs) for the commodities that are the representative uses (i.e. wheat, barley, rye, oats, triticale, maize) are used, the max. theoretical maximum daily intake (TMDI) corresponds to 23% of the ADI (WHO cluster diet B) and the highest acute exposure to 1.1% of the ARfD (wheat, UK 4- to 6-year-old child). The consumer risk for animal products could not be finalised since, the identity and transfer of residues and their levels in animal commodities for human consumptions have not been elucidated.

Considering the representative uses on cereals and the maximum application rate applied: the non-dietary exposure (short to long-term) for operators were up to 18% of the acceptable operator exposure level (AOEL) with the risk mitigation measures. Under this situation, the margin of exposure is 7,561 and 2,520 for the no observed adverse effect level (NOAEL) and point of departure (PoD), respectively, for the developmentality toxicity effect. The estimates for acute exposure were up to 30% of the acute acceptable operator exposure level (AAOEL) with risk mitigation measures. Considering this scenario the margin of exposure is 1,035 and 345 for the NOAEL and PoD, respectively, for the developmentality toxicity effect. The exposure estimates for workers were up to 107% of the AOEL with the use of workwear, and a margin of exposure of 1,246 and 415 for the NOAEL and PoD, respectively, for the developmentality toxicity effect. The exposure estimates for residents and bystanders were up to 185% of the AOEL and 39% of the AAOEL, taking into account refined dislodgeable foliar residue (DFR) value, a buffer zone of 10 m and drift reduction nozzles. Under this situation, the margin of acute exposure was 786 and 262 for the NOAEL and PoD, respectively, for the developmentality toxicity
effect, and for short- to long-term exposure was 721 and 240 for the NOAEL and PoD, respectively, for the developmental toxicity effect. Considering the representative uses on cereals and minimum application rate, the exposure estimates are very similar to the ones considered for maximum application rates, since dermal absorption values are higher when considering lower application rates.
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Background

Commission Implementing Regulation (EU) No 844/2012 (hereinafter referred to as the Regulation) lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012. Bromoxynil is one of the active substances listed in Regulation (EU) No 686/2012. The European Food Safety Authority (EFSA) finalised a conclusion on the peer review of the pesticide risk assessment of the active substance bromoxynil according to Article 13 of Regulation (EU) No 844/2012 on 14 June 2017 (EFSA, 2017a) and provided its conclusion to the European Commission.

Annex II of Regulation (EU) No 1107/2009 provides in its points 3.6.3, 3.6.4 and 3.6.5 that active substances classified on the basis of Regulation (EC) No 1272/2008 as carcinogen category 1A or 1B or toxic for reproduction category 1A or 1B, or having endocrine-disrupting properties which may cause adverse effects on humans cannot be approved unless the exposure of humans to that active substance in a plant protection product, under realistic proposed conditions of use, is negligible. These conditions under which negligible exposure is assumed is precondition for approval of substances in accordance with Article 4 of the Regulation (EU) No 1107/2009 read in combination with these points.

The European Commission shall propose a decision on renewal/non-renewal of approval for active substances considered under Regulation (EU) No 1107/2009 taking into account the approval criteria of Annex II, points 3.6.3, 3.6.4 and 3.6.5 of that Regulation.

In 2017, during the peer review for the renewal of approval (EFSA, 2017a), EFSA proposed to classify bromoxynil (and its esters) as toxic for reproduction category 1B, leading to a critical area of concern with regard to the approval criteria of Annex II, Point 3.6.4. of Regulation (EC) No 1107/2009. In addition, bromoxynil and its esters are currently classified as toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and toxic effects on the endocrine organs were observed in the data available during the peer review; therefore, the conditions of the interim provisions of Annex II, Point 3.6.5 of Regulation (EC) No 1107/2009 concerning human health for the consideration of endocrine-disrupting properties may be met.

The classification proposed during the peer review triggers the lack of compliance with the approval criteria set out in points 3.6.2–3.6.4 but this was not known by the applicant at the time of the dossier submission. As a consequence, the applicant did not submit information in its dossier to demonstrate that exposure of humans to the substance, under realistic conditions of use, can be considered negligible. Therefore, in order to inform the decision-making process, the European Commission invited the applicant Bayer CropScience, on behalf of the Bromoxynil Task Force, to provide further information to demonstrate that the exposure of humans to bromoxynil is negligible under realistic conditions of use. The European Commission then requested the rapporteur Member State (RMS), France, to carry out an evaluation of this information and to submit its assessment in the format of an addendum to EFSA. By means of a general mandate received on 13 January 2016, the European Commission requested EFSA to conduct a peer review and provide its conclusions on particular active substances, to be communicated on an ad hoc basis, on whether exposure of humans to an active substance, under realistic conditions of use, can be considered negligible, taking into account the adoptedTechnical guidance on points 3.6.3 to 3.6.5 of Annex II to Regulation (EC) No 1107/2009, in particular regarding the demonstration of negligible exposure to an active substance in a plant protection product under realistic conditions of use or, if not yet adopted, the latest version available of PAFF Section Pesticide Legislation (SANCO/2014/12096). EFSA should deliver its conclusions within 3 months from the date of receipt of the assessment by the RMS, unless otherwise requested by separate mandate whereby additional time may be given to complete the work and deliver the conclusions depending on the complexity of the specific case.

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1 Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252,19.9.2012, p. 26-32.

2 Regulation (EC) No 1107/2009 of 21 October 2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

3 Commission Implementing Regulation (EU) No 686/2012 of 26 July 2012 allocating to Member States, for the purposes of the renewal procedure, the evaluation of the active substances whose approval expires by 31 December 2018 at the latest. OJ L 200, 27.7.2012, p. 5-10.

4 Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1-1355.
The applicant, Bayer CropScience on behalf of the Bromoxynil Task Force, submitted an updated dossier in 12 January 2018, which was evaluated by the RMS, France, in the form of an addendum to the renewal assessment report (RAR) (France, 2018). The RMS provided its addendum to the RAR on 26 June 2018 to EFSA. EFSA distributed the addendum to Member States for comments on 27 June 2018, and provided comments as well. EFSA collated all comments and provided its scientific view on the comments received.

The addendum and the compiled commenting table were discussed at an expert consultation in the area of toxicology in September 2018. Details of the issues discussed, together with the outcome of these discussions were recorded in the meeting report.

A final consultation on the conclusions arising from the peer review took place with Member States via a written procedure in October 2018.

The conclusions laid down in this report were reached on the basis of the peer review of the RMS’s evaluation of the negligible exposure data submitted. A key supporting document to this conclusion is the peer review report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the compilation of comments to the conclusion. The peer review report (EFSA, 2018) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the addendum to the RAR;
- the report of the scientific consultation with Member State experts;
- the comments received on the draft EFSA conclusion.

Given the importance of the addendum to the RAR (France, 2018) and the peer review report, these documents are considered as background documents to this conclusion.

It is recommended that this conclusion report and its background documents would not be accepted to support any registration outside the European Union (EU) for which the applicant has not demonstrated to have regulatory access to the information on which this conclusion report is based.

The active substance and the formulated product

Bromoxynil is the ISO common name for 3,5-dibromo-4-hydroxybenzonitrile (IUPAC). The esters of bromoxynil are derivatives of this active substance. Bromoxynil butyrate, bromoxynil heptanoate and bromoxynil octanoate are the modified ISO common names for 2,6-dibromo-4-cyanophenyl butyrate, 2,6-dibromo-4-cyanophenyl heptanoate and 2,6-dibromo-4-cyanophenyl octanoate (IUPAC), respectively. The representative formulated product for the evaluation was ‘Bromoxynil-octanoate EC 327.5 G’, an emulsifiable concentrate (EC) containing 327.5 g/L bromoxynil octanoate (equivalent to 225 g/L pure bromoxynil). The representative uses evaluated in the peer review for renewal of approval were spray applications in maize, spring barley, spring wheat and oats, and in winter wheat, winter barley, rye and triticale to control dicotyledonous weeds. Full details of the Good Agricultural Practice (GAP) can be found in the Appendix A.

Conclusions of the evaluation

The applicant has submitted to the Commission information to demonstrate that the exposure of humans to bromoxynil can be considered negligible under the proposed condition of use.

The assessment of the information was presented in an addendum to the RAR (France, 2018) prepared according to the draft Technical Guidance Document on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (points 3.6.3 to 3.6.5 and 3.8.2 of Annex II of Regulation (EC) No 1107/2009) SANCO/2014/12096 (European Commission, 2015).

1. Negligible exposure to humans

The following guidance documents were followed in the production of this conclusion: SANCO/2014/12096 (European Commission, 2015) and EFSA Guidance on the assessment of exposure of operators, workers, residents and bystanders (EFSA, 2014).

The reference values for bromoxynil agreed during the peer review (EFSA, 2017a,b) are presented in Table 1.
The no observed adverse effect level (NOAEL) for the critical effect (developmental toxicity) is 4 mg/kg body weight (bw) per day and the point of departure (PoD) for developmental toxicity taking into account an uncertainty factor of 3 due to severity of developmental is 1.33 mg/kg bw per day.

1.1. Dietary exposure

Data gaps identified during the renewal process of bromoxynil (EFSA, 2017a), are still valid since no new data was submitted. In the absence of fully reliable metabolism studies in cereals that is sufficiently representative of the requested GAPs, the residue definition for risk assessment in plant as bromoxynil and its esters expressed as bromoxynil is provisional for feed items (cereals straw, maize forage/silage, maize stover). Specifically, in the feed items, the relevant residue could not be concluded since the different bromoxynil esters showed a different metabolic pattern in wheat, maize and alfalfa (see detailed assessment in EFSA, 2017a,b). Moreover, metabolites identification in wheat straw at harvest was not conducted but is essential to evaluate livestock exposure with regard to the representative uses. For grains, based on the overall metabolism data, negligible translocation of residues was observed; thus, it was reasonably assumed that the total radioactive residues (TRRs) in cereal grains are expected to be very low.

As regards the residue levels in field trials provided in cereal grains (maize, wheat, rye, barley and triticale), they were all below 0.01 mg/kg, while in cereal straw they were up to 0.02 mg/kg; hence, exceeding the limit of quantification (LOQ) of 0.01 mg/kg. All the trials (grain and feed items) were analysed according to the provisional residue definition, bromoxynil and its esters. It should be noted that these results cover the representative GAPs on cereals for grain production only. In the cereal forage, the residue levels were measured up to 0.54 mg/kg in wheat and 0.69 mg/kg in barley.

In view of identified shortcomings with regard to feed items, the livestock exposure assessment is provisional and may increase once the relevant residues in feed items have been fully elucidated. Hence, no conclusion could be derived on the identity and transfer of residues and their levels in animal commodities for human consumptions.

A provisional consumer dietary risk assessment was conducted with EFSA PRIMo rev.2 and considering the levels of residue in cereals grain (maize, wheat, rye, barley and triticale) at 0.01 mg/kg. Long-term or short-term intake concerns were not identified for the consumers since the highest chronic and highest acute intakes accounted for 3.8% of the acceptable daily intake (ADI) (WHO Cluster diet B) and 1.1% of the acute reference dose (ARfD) (for wheat). If the currently established MRLs for the commodities that are the representative uses (i.e. wheat, barley, oats, rye, triticale, maize) are used, the max. theoretical maximum daily intake (TMDI) corresponds to 23% of the ADI (WHO cluster diet B) and highest acute exposure to 1.1% of the ARfD (wheat, UK 4- to 6-year-old child). The consumer risk assessment for animal products could not be finalised based on the available data.

1.2. Non-dietary exposure

‘Bromoxynil octanoate EC 327.5 G’ is an emulsion concentrate containing 327.5 g bromoxynil octanoate/L (equivalent to 225 g bromoxynil/L). The representative uses are spray applications in maize, spring barley, spring wheat and oats and in winter wheat, winter barley, rye and triticale to control dicotyledonous weeds. Applications of ‘BXO EC 327.5 G’ will be achieved via field crop sprayers.

The dermal absorption values of bromoxynil-octanoate in ‘Bromoxynil-octanoate EC 327.5 G’ were agreed during the peer review (EFSA, 2017a,b) as being: 3% for the concentrate, 14% for the 1.23 g BXO/L dilution and of 21% for the 0.82 g BXO/L dilution (in vitro human dermal absorption study).

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**Table 1: Reference values for bromoxynil (EFSA, 2017a)**

|                | Value (mg/kg bw (per day)) | Study               | Uncertainty factor |
|----------------|---------------------------|---------------------|--------------------|
| ADI(a),(d)     | 0.003                     | Dog, 1-year         | 100                |
| ARfD(a),(d)    | 0.013                     | Rat, developmental  | 300(b)             |
| AOE(a),(d)     | 0.003(c)                  | Dog, 1-year         | 100                |
| AAOE(a),(d)    | 0.013(c)                  | Rat, developmental  | 300(b)             |

bw: body weight.

(a): ADI: acceptable daily intake; ARfD: acute reference dose; AOE: acceptable operator exposure level (short to long term exposure); AAOE: acute acceptable operator exposure level (acute exposure).

(b): An extra factor of 3 is proposed due to severity of developmental effects.

(c): No correction for oral absorption needed.

(d): Expressed as bromoxynil.
The non-dietary exposure assessment on bromoxynil was discussed during the Pesticides Peer Review Experts’ Meeting 182 (EFSA, 2018). The experts agreed with the RMS on the dermal absorption values to be used for the different exposure groups and on the non-acceptability of the large outdoor wind tunnel study to refine vapour concentration in air. Regarding the refinement for workers exposure to include gloves (a transfer coefficient (TC), is not available in the EFSA guidance) the experts proposed to use a TC of 1,250 cm²/h (10% of general TC of 12,500 cm²/h for crop inspection activities) for the use of gloves. However, it was acknowledged that the outcome of the exposure estimates as presented in Tables 2 and 3 will not significantly change since the TC when using work wear without considering gloves is 1,400 cm²/h (i.e. very similar to the proposed TC using gloves).

First tier assessment:

Exposure estimates have been provided for operators, workers, bystanders and residents, for the representative uses on cereals considering the maximum and minimum application rate and compared to the acceptable operator exposure level (AOEL) and acute acceptable operator exposure level (AAOEL). The exposure assessment for residents also covers longer term exposure for bystanders. The acute exposure assessment for the bystanders also covers acute exposure scenarios for the residents. The results, including possible risk mitigation measures, are presented in Tables 2 and 3 for the maximum and minimum application rate, respectively.

Second tier assessment:

Considerations were also given to the margin of exposure (MoE) between non-dietary exposure and the NOAEL and PoD for the critical effects (i.e. 4 and 1.33 mg/kg bw per day, respectively). The results, including possible risk mitigation measures, are also presented in Table 2 and Table 3 for the maximum and minimum application rate, respectively.

Table 2: Non-dietary exposure scenarios and margin of exposure (MoE) – Use in cereals 1.5 L BXO EC 327.5 G/ha 491.25 g BXO/ha eq. to 337.5 g BXP/ha

| EFSA Model       | Risk mitigation measures                                      | Systemic dose (mg/kg bw per day) | % AOEL or % AAOEL(a) | MoE to NOAEL(b) | MoE to PoD(c) |
|------------------|-------------------------------------------------------------|----------------------------------|----------------------|----------------|---------------|
| OPERATOR         |                                                             |                                   |                      |                |               |
| Short- to long-term exposure | Work wear (arms, body and legs covered)                     | 0.028266                         | 942                  | 142            | 47            |
|                  | Work wear + gloves mixing/loading (M/L) and application (A)  | 0.001608                         | 54                   | 2,488          | 829           |
|                  | Work wear + gloves M/L and A + drift reducing nozzles       | 0.000979                         | 33                   | 4,086          | 1,362         |
|                  | Work wear + gloves M/L and A + drift reducing nozzles + hood and visor | 0.000529                         | 18                   | 7,561          | 2,520         |
| Acute exposure   | Work wear (arms, body and legs covered)                     | 0.127775                         | 983                  | 31             | 10            |
|                  | Work wear + gloves mixing/loading (M/L) and application (A)  | 0.017562                         | 135                  | 228            | 76            |
|                  | Work wear + gloves M/L and A + drift reducing nozzles       | 0.006170                         | 47                   | 648            | 216           |
|                  | Work wear + gloves M/L and A + drift reducing nozzles + hood and visor | 0.003864                         | 30                   | 1,035          | 345           |
| WORKER           |                                                             |                                   |                      |                |               |
| Inspection, irrigation | Work wear                                               | 0.006615                         | 221                  | 605            | 202           |
|                  | Work wear, refined DFR value                              | 0.0032105                        | 107                  | 1,246          | 415           |
| EFSA Model | Risk mitigation measures | Systemic dose (mg/kg bw per day) | % AOEL or % AAOEL<sup>(a)</sup> | MoE to NOAEL<sup>(b)</sup> | MoE to PoD<sup>(c)</sup> |
|------------|--------------------------|---------------------------------|---------------------------------|--------------------------|--------------------------|
| **Bystander** |                          |                                 |                                 |                          |                          |
| Child:     | Spray drift              | None                            | 0.019366                        | 149                      | 207                      | 69                      |
|            | Vapour                   |                                 | 0.001070                        | 8                        | 3,738                    | 1,246                   |
|            | Surface deposits         |                                 | 0.002806                        | 22                       | 1,426                    | 475                     |
|            | Entry in crops           |                                 | 0.007973                        | 61                       | 502                      | 167                     |
| Adult:     | Spray drift              |                                 | 0.005228                        | 40                       | 765                      | 255                     |
|            | Vapour                   |                                 | 0.000230                        | 2                        | 17,391                   | 5,797                   |
|            | Surface deposits         |                                 | 0.000971                        | 7                        | 4,119                    | 1,373                   |
|            | Entry in crops           |                                 | 0.004430                        | 34                       | 903                      | 301                     |
| Child:     | Spray drift              | 10 m buffer zone                 | 0.010177                        | 78                       | 393                      | 131                     |
|            | Vapour                   |                                 | 0.001070                        | 8                        | 3,738                    | 1,246                   |
|            | Surface deposits         |                                 | 0.000627                        | 5                        | 6,380                    | 2,127                   |
|            | Entry in crops           |                                 | 0.007973                        | 61                       | 502                      | 167                     |
| Adult:     | Spray drift              |                                 | 0.002068                        | 16                       | 1,934                    | 645                     |
|            | Vapour                   |                                 | 0.000230                        | 2                        | 17,391                   | 5,797                   |
|            | Surface deposits         |                                 | 0.000217                        | 2                        | 18,433                   | 6,144                   |
|            | Entry in crops           |                                 | 0.004430                        | 34                       | 903                      | 301                     |
| Child:     | Spray drift              | 10 m buffer zone + drift         | 0.005089                        | 39                       | 786                      | 262                     |
|            | reduction nozzles        |                                 |                                 |                          |                          |                          |
|            | Vapour                   |                                 | 0.001070                        | 8                        | 3,738                    | 1,246                   |
|            | Surface deposits         |                                 | 0.000314                        | 2                        | 12,739                   | 4,246                   |
|            | Entry in crops           |                                 | 0.007973                        | 61                       | 502                      | 167                     |
| Adult:     | Spray drift              |                                 | 0.001034                        | 8                        | 3,868                    | 1,289                   |
|            | Vapour                   |                                 | 0.000230                        | 2                        | 17,391                   | 5,797                   |
|            | Surface deposits         |                                 | 0.000109                        | 1                        | 36,697                   | 12,232                  |
|            | Entry in crops           |                                 | 0.004430                        | 34                       | 903                      | 301                     |
| Child:     | Spray drift              | 10 m buffer zone + drift         | 0.005089                        | 39                       | 786                      | 262                     |
|            | reduction nozzles +      |                                 |                                 |                          |                          |                          |
|            | refined DFR value        |                                 |                                 |                          |                          |                          |
|            | Vapour                   |                                 | 0.001070                        | 8                        | 3,738                    | 1,246                   |
|            | Surface deposits         |                                 | 0.000314                        | 2                        | 12,739                   | 4,246                   |
|            | Entry in crops           |                                 | 0.003870                        | 30                       | 1,034                    | 345                     |
| Adult:     | Spray drift              |                                 | 0.001034                        | 8                        | 3,868                    | 1,289                   |
|            | Vapour                   |                                 | 0.000230                        | 2                        | 17,391                   | 5,797                   |
|            | Surface deposits         |                                 | 0.000108                        | 1                        | 3,7037                   | 12,346                  |
|            | Entry in crops           |                                 | 0.002150                        | 17                       | 1,860                    | 620                     |
| **Resident** |                          |                                 |                                 |                          |                          |                          |
| Child:     | None                     |                                 | 0.012820                        | 427                      | 312                      | 104                     |
| Adult       |                          |                                 | 0.004962                        | 165                      | 806                      | 269                     |
| Child:     | 10 m buffer zone         |                                 | 0.010207                        | 340                      | 392                      | 131                     |
| Adult:     |                          |                                 | 0.004294                        | 143                      | 932                      | 311                     |
| Child:     | 10 m buffer zone + drift |                                 | 0.008817                        | 294                      | 454                      | 151                     |
|            | reduction nozzles        |                                 | 0.004028                        | 134                      | 993                      | 331                     |
| Adult:     |                          |                                 | 0.005545                        | 185                      | 721                      | 240                     |
| Child:     | 10 m buffer zone + drift |                                 | 0.002210                        | 74                       | 1,810                    | 603                     |
|            | reduction nozzles +      |                                 |                                 |                          |                          |                          |
|            | refined DFR value        |                                 |                                 |                          |                          |                          |

bw: body weight; DFR: dislodgable foliar residue.

(a): AOEL: acceptable operator exposure level (short- to long-term exposure); AAOEL: acute AOEL (acute exposure).

(b): MoE: margin of exposure for reproductive toxicity being the ratio between critical systemic NOAEL and estimated exposure.

(c): MoE: margin of exposure for reproductive toxicity being the ratio between critical PoD and estimated exposure.
Table 3: Non-dietary exposure scenarios and margin of exposure (MoE) – Use in cereals 1 L BXO EC 327.5 G/ha – 337.5 g BXO/ha eq. to 225 g Bromoxynil/ha

| EFSA Model       | Risk mitigation measures                                                                 | Systemic dose (mg/kg bw per day) | % AOEL or % AAOEL\(^{(a)}\) | MoE to NOAEL\(^{(b)}\) | MoE to PoD\(^{(c)}\) |
|------------------|----------------------------------------------------------------------------------------|----------------------------------|------------------------------|------------------------|------------------------|
| **OPERATOR**     |                                                                                        |                                  |                              |                        |                        |
| Short- to long-term exposure | Work wear (arms, body and legs covered)                                                                 | 0.022313                         | 744                          | 179                    | 60                     |
|                  | Work wear + gloves mixing/loading (M/L) and application (A)                              | 0.001457                         | 49                           | 2,745                  | 915                    |
|                  | Work wear + gloves M/L and A + drift reducing nozzles                                    | 0.000742                         | 25                           | 5,391                  | 1,797                  |
|                  | Work wear + gloves M/L & A + drift reducing nozzles + hood and visor                      | 0.000435                         | 15                           | 9,195                  | 3,065                  |
| Acute exposure   | Work wear                                                                               | 0.109614                         | 843                          | 36                     | 12                     |
|                  | Work wear + gloves mixing/loading (M/L) and application (A)                              | 0.020394                         | 157                          | 196                    | 65                     |
|                  | Work wear + gloves M/L and A + drift reducing nozzles                                    | 0.004448                         | 34                           | 899                    | 300                    |
|                  | Work wear + gloves M/L and A + drift reducing nozzles + hood and visor                    | 0.002897                         | 22                           | 1381                   | 460                    |
| **WORKER**       |                                                                                        |                                  |                              |                        |                        |
| Inspection, irrigation | Work wear                                                                                    | 0.006615                         | 221                          | 605                    | 202                    |
|                  | Work wear, refined DFR value                                                             | 0.0032105                        | 107                          | 1,246                  | 415                    |
| **Bystander**    |                                                                                        |                                  |                              |                        |                        |
| Child:           | Spray drift None                                                                         | 0.019282                         | 148                          | 207                    | 69                     |
|                  | Vapour                                                                                  | 0.001070                         | 8                            | 3,738                  | 1,246                  |
|                  | Surface deposits                                                                         | 0.002567                         | 20                           | 1,558                  | 519                    |
|                  | Entry in crops                                                                           | 0.007973                         | 61                           | 502                    | 167                    |
| Adult:           | Spray drift                                                                             | 0.005222                         | 40                           | 766                    | 255                    |
|                  | Vapour                                                                                  | 0.000230                         | 2                            | 17,391                 | 5,797                  |
|                  | Surface deposits                                                                         | 0.000971                         | 7                            | 4,119                  | 1,373                  |
|                  | Entry in crops                                                                           | 0.004430                         | 34                           | 903                    | 301                    |
| Child:           | Spray drift 10 m buffer zone                                                            | 0.010120                         | 78                           | 395                    | 132                    |
|                  | Vapour                                                                                  | 0.001070                         | 8                            | 3,738                  | 1,246                  |
|                  | Surface deposits                                                                         | 0.000574                         | 4                            | 6,969                  | 2,323                  |
|                  | Entry in crops                                                                           | 0.007973                         | 61                           | 502                    | 167                    |
| Adult:           | Spray drift                                                                             | 0.002062                         | 16                           | 1,940                  | 647                    |
|                  | Vapour                                                                                  | 0.000230                         | 2                            | 17,391                 | 5,797                  |
|                  | Surface deposits                                                                         | 0.000109                         | 1                            | 36,697                 | 12,232                 |
|                  | Entry in crops                                                                           | 0.004430                         | 34                           | 903                    | 301                    |
2. Negligible exposure to non-target organisms

The draft Technical Guidance on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (SANCO/2014/12096 (European Commission, 2015)) does not give any guidance for consideration of negligible exposure for non-target organisms. Therefore, the assessment of potential negligible exposure to non-target organisms is not assessed in this conclusion.

### References

EFSA (European Food Safety Authority), 2014. EFSA Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp. https://doi.org/10.2903/j.efsa.2014.3874

EFSA (European Food Safety Authority), 2017b. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance bromoxynil (variant evaluated bromoxynil octanoate). Available online: www.efsa.europa.eu

EFSA (European Food Safety Authority), 2018. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the bromoxynil in light of negligible exposure data submitted. EFSA Journal 2018;16(11):5490, 20 pp. https://doi.org/10.2903/j.efsa.2018.5490

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| EFSA Model | Risk mitigation measures | Systemic dose (mg/kg bw per day) | % AOEL or % AAOEL\(^{(a)}\) | MoE to NOAEL\(^{(b)}\) | MoE to PoD\(^{(c)}\) |
|------------|-------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Child:     | Spray drift             | 10 m buffer zone + drift reduction nozzles | 0.005060 | 39 | 791 | 264 |
|            | Vapour                  | 0.001070 | 8 | 3,738 | 1,246 |
|            | Surface deposits        | 0.000287 | 2 | 13,937 | 4,646 |
|            | Entry in crops          | 0.007973 | 61 | 502 | 167 |
| Adult:     | Spray drift             | 0.001031 | 8 | 3,880 | 1,293 |
|            | Vapour                  | 0.000230 | 2 | 17,391 | 5,797 |
|            | Surface deposits        | 0.000109 | 1 | 36,697 | 12,232 |
|            | Entry in crops          | 0.004430 | 34 | 903 | 301 |
| Child:     | Spray drift             | 10 m buffer zone + drift reduction nozzles + refined DFR value | 0.005060 | 39 | 791 | 264 |
|            | Vapour                  | 0.001070 | 8 | 3,738 | 1,246 |
|            | Surface deposits        | 0.000287 | 2 | 13,937 | 4,646 |
|            | Entry in crops          | 0.003870 | 30 | 1,034 | 345 |
| Adult:     | Spray drift             | 0.001031 | 8 | 3,880 | 1,293 |
|            | Vapour                  | 0.000230 | 2 | 17,391 | 5,797 |
|            | Surface deposits        | 0.000109 | 1 | 36,697 | 12,232 |
|            | Entry in crops          | 0.002150 | 17 | 1,860 | 620 |

bw: body weight; DFR: dislodgeable foliar residue.

(a): AOEL: acceptable operator exposure level (short to long term exposure); AAOEL: acute AOEL (acute exposure).

(b): MoE: margin of exposure for reproductive toxicity being the ratio between critical systemic NOAEL and estimated exposure.

(c): MoE: margin of exposure for reproductive toxicity being the ratio between critical PoD and estimated exposure.
European Commission, 2015. Draft Technical Guidance Document on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (points 3.6.3 to 3.6.5, and 3.8.2 of Annex II of Regulation (EC) No 1107/2009). SANCO/2014/12096), November 2015

France, 2018. Addendum to the Renewal Assessment Report (RAR) on the active substance bromoxynil prepared by the rapporteur Member State France according to the Draft Technical Guidance Document on assessment of negligible exposure of an active substance in a plant protection product under realistic conditions of use (points 3.6.3 to 3.6.5, and 3.8.2 of Annex II of Regulation (EC) No 1107/2009; SANCO-2014-12096), June 2018. Available online: www.efsa.europa.eu

Abbreviations

a.s. active substance
ADI acceptable daily intake
AOEL acceptable operator exposure level
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
DAR draft assessment report
DFR dislodgeable foliar residue
EC emulsiﬁable concentrate
EEC European Economic Community
GAP Good Agricultural Practice
ISO International Organization for Standardization
IUPAC International Union of Pure and Applied Chemistry
LOQ limit of quantiﬁcation (determination)
M/L mixing and loading
MoE margin of exposure
MRL maximum residue level
NOAEL no observed adverse effect level
OECD Organisation for Economic Co-operation and Development
PHI preharvest interval
PoD point of departure
RAR renewal assessment report
RMS rapporteur Member State
TC transfer coefﬁcient
TMDI theoretical maximum daily intake
WHO World Health Organization
# Appendix A – List of representative uses evaluated for negligible exposure

| Crop and/or situation(a) | Member State or Country | Product name | F G or I(b) | Pests or Group of pests controlled(c) | Formulation | Application | Application rate per treatment | PHI (days) (m) | Remarks |
|--------------------------|--------------------------|--------------|-------------|---------------------------------------|-------------|------------|------------------------------|----------------|---------|
| Maize/corn (ZEAMX)      | EU                       | Bromoxynil-octanoate EC 327.5 G (327.5 g/L) | F           | Dicotyledonous weed plants (TTTDD)    | EC          | Spraying   | BBCH 12-19 (spring)          | 150–400        | 0.0819–0.3275 Rate per ha given as bromoxynil octanoate rate which is equivalent to 225–337.5 g bromoxynil/ha |
|                         |                          |              |             |                                       |             |            |                              |                | 90      |
| Spring Barley, Spring Wheat, Oats | EU                       | Bromoxynil-octanoate EC 327.5 G (327.5 g/L) | F           | Dicotyledonous weed plants (TTTDD)    | EC          | Spraying   | BBCH 13-32 (spring)          | 150–400        | 0.0819–0.3275 Rate per ha given as bromoxynil octanoate rate which is equivalent to 225–337.5 g bromoxynil/ha |
|                         |                          |              |             |                                       |             |            |                              |                | 75      |
| Crop and/or situation(a) | Member State or Country | Product name | F or G or I(b) | Pests or Group of pests controlled(c) | Formulation | Application | Application rate per treatment | PHI (days) | Remarks: |
|--------------------------|-------------------------|--------------|----------------|-------------------------------------|-------------|-------------|--------------------------------|-----------|---------|
| Winter Barley, Winter Wheat, Rye, Triticale | EU | Bromoxynil-octanoate EC 327.5 G (327.5 g/L) | F | Dicotyledonous weed plants (TTTDD) | EC | Bromoxynil octanoate: 327.5 g/L (equivalent to 225 g/L bromoxynil) | Spraying BBCH 13-32 (autumn or spring) | 1 | n.a. | 0.0819–0.3275 | 150–400 | 0.3275–0.4913 | 75 | Rate per ha given as bromoxynil octanoate rate which is equivalent to 225–337.5 g bromoxynil/ha |

a.s.: active substance; PHI: preharvest interval; EC: emulsifiable concentrate; BBCH: growth stages of mono- and dicotyledonous plants.
(a): For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure).
(b): Outdoor or field use (F), glasshouse application (G) or indoor application (I).
(c): e.g. biting and sucking insects, soil born insects, foliar fungi, weeds.
(d): Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench.
(h): Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated.
(j): Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application.
(k): The minimum and maximum number of application possible under practical conditions of use must be provided.
(l): PHI: minimum preharvest interval.
(m): Remarks may include: Extent of use/economic importance/restrictions.