EUROPEAN CHEMICALS AGENCY

ECHA accordance check report on the dossier proposing harmonised classification and labelling (CLH) for glyphosate (ISO); N-(phosphonomethyl)glycine

glyphosate (ISO); N-(phosphonomethyl)glycine	
Type of substance:	Active substance in Plant Protection Products under the Annex I Renewal (AIR) process (Regulation (EC) No. 1141/2010 or Regulation (EC) No.844/2012)
Date of submission:	17/03/2016
Submission number:	EM011055-54
Dossier submitter	
Submitting Member State:	Germany
Contact person:	[redacted]
Email of the contact person:	[redacted]
ECHA Secretariat	
Scientific dossier manager(s) (SDM):	[redacted]
Email of SDM:	[redacted]@echa.europa.eu [redacted]@echa.europa.eu
Substance identity (SID) assessor:	[redacted]
Accordance check report completed on (date):	04/05/2016

Annex 1: Accordance check report for glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

1. Hazard classes open for comments during public consultation and subject to RAC evaluation

Based on the information provided in the CLH report and the type of proposal and substance the following hazard classes will be opened for comments during public consultation (PC) and evaluated by RAC:

- All hazard classes (human health and the environment), with the exception of respiratory sensitisation, aspiration hazard or hazardous to the ozone layer

In case of disagreement or for any clarification related to the hazard classes that will be opened for comments and evaluated by RAC, please do not hesitate to contact the ECHA Scientific Dossier Managers.

Please also see the comment under Section 4.7 of this report.

Please note that all text that has been added to this report and to the tracked changes version of the CLH report relative to the previous (draft) versions have been highlighted in yellow.

2. Outcome of SID assessment (Annex VI, Part 2 CLP)

Based on the information provided in the CLH report, the ECHA SID Team concludes that the International Chemical Identification for the substance Annex VI entry is the following:

Index No	International Chemical Identification	EC No	CAS No
607-315-00-8	glyphosate (ISO); N-(phosphonomethyl)glycine	213-997-4	1071-83-6

For any clarification related to the International Chemical Identification, please do not hesitate to contact ECHA via the Classification functional mailbox (classification@echa.europa.eu) or the ECHA Scientific Dossier Managers.

2.1 The substance can be correctly and unambiguously identified based on the information contained in the CLH report	**Yes** ☒	**No** ☐

The CLH report and IUCLID dossier refer only to N-(phosphonomethyl)glycine.

ECHA notes the following:

- This dossier does not cover any salt of Glyphosate.
- the DAR attached in the IUCLID dossier includes information on salts of Glyphosate in the substance identification section
- Annex VI of CLP includes entry 015-184-00-8 "Salts of glyphosate, with the exception of those specified elsewhere in this Annex"

It would be useful if the dossier submitter could clarify if any action is foreseen in relation to this group of salts.

Annex 1: Accordance check report for glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

Recommended information/revisions:

Part A, table 1:

- The EC name should be amended to "Glyphosate"

Part B, table 4:

- The EC name should be amended to "Glyphosate"
- The Chemical Abstract Index name should be amended to "Glycine, *N*-(phosphonomethyl)-"

Confidential Annex of the CLH report, page 2 - Impurities and Additives table:

- It seems there is a clerical error in the unit reported for "specified limit". The unit should be amended to g/kg instead of [% (w/w)]

2.2 The substance can be correctly and unambiguously identified based on the information contained in the IUCLID dossier	**Yes** ☒	**No** ☐

Recommended information/revisions:

Section 1.1:

- The EC information is missing. The EC number and EC name should be included in the corresponding fields.

2.3 The composition of the test substance is adequately specified	**Yes** ☐	**No** ☐	**Not examined** ☒

2.4 The test substance identity is the same as the substance proposed for CLH	**Yes** ☐	**No** ☐	**Not examined** ☒

2.5 The substance identity in the CLH proposal covers the substance identity in the corresponding REACH registration dossiers	**Yes** ☐	**No** ☐	**N/A** ☒

No registrations as of the date of this report.

3. REACH registration dossiers and/or DAR/CAR (Annex VI, Part 2 to CLP)

3.1 There is/are (a) registration dossier(s) available for the substance (checked on 24/3/2016)	**Yes** ☐	**No** ☒	

3.2 There is a DAR available for the substance (checked on 24/3/2016)	**Yes** ☒	**No** ☐	**N/A** ☐
3.3 There is a CAR available for the substance (checked on 24/3/2016)	**Yes** ☐	**No** ☒	**N/A** ☐
3.4 The information from registration dossiers and/or DAR/CAR considered relevant for the proposed classification was assessed and the outcome of the assessment is documented in the CLH report	**Yes** ☒	**No** ☐	**N/A** ☐

Required information/revisions: None

Recommended information/revisions: None

4. CLH report (Annex VI, Part 2 CLP)

4.1 The CLH report is prepared according to the CLH report format	**Yes** ☒	**No** ☐

Required information/revisions: None

Recommended information/revisions:

In Part A Section 2.4 of the CLH report is missing. It should include the heading "Current self-classification and labelling". This section should summarise any self-classifications for this substance from the C&L inventory (http://echa.europa.eu/information-on-chemicals/cl-inventory-database) that deviate from the harmonised classification (if any). Please complete this section accordingly.

4.2 The CLH report correctly specifies the classification and labelling (Class and Category Code(s), Hazard statement Code(s), Pictogram, Signal Word Code(s), Hazard statement Code(s), Suppl. Hazard statement Code(s), Specific Conc. Limits, M-factors Notes, affected organs/specific effects/route of exposure) in accordance with the CLP Regulation (EC) No 1272/2008	**Yes** ☐	**No** ☒

Required information/revisions:
The pictogram GHS05 needs to be added to the "labelling" section, under Table 3.

Recommended information/revisions: None

4.3 The CLH report systematically provides sufficient details of the available hazard information relevant for the proposed classification	**Yes** ☒	**No** ☐

Required information/revisions: None

Recommended information/revisions:

It is recommended that the literature search strategy, scope and inclusion/exclusion criteria for the CMR studies be summarised, particularly in view of the reference to the toxicological database for glyphosate being extremely large, that the studies have come from a great number of sources and that they all have been taken into consideration. Although there is no CLP Guidance for the inclusion of data from public literature, it is recommended that the principles from the EFSA Guidance (2011) on "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009" be considered (http://www.efsa.europa.eu/fr/efsajournal/pub/2092).

It would be helpful to include, for example in Table 16, indication of whether or not the findings were significant.

Please ensure that the weight of evidence (WoE) is argued clearly for all endpoints. As you know, WoE can generally be described as a stepwise process/approach of collecting evidence and weighing them to reach a conclusion on a particular problem formulation with (pre)defined degree of confidence. For your consideration, ECHA is developing a general WoE guidance whereby the following steps will be developed:

1. Problem formulation
2. Collection of lines of evidence (documentation of search strategy & documentation/reporting of evidence)
3. Assessment of quality of individual evidence (reliability, relevance/adequacy)
4. a) WoE analysis & b) Documentation(Integration and Assessment of overall evidence (consistency, specificity))
5. Confidence levels (qualitative and/or quantitative)
6. Conclusion / Remaining uncertainty (completeness and adequacy for purpose)

It is recommended that the epidemiological data be tabulated.

Please note the observations of the rapporteurs in Annex 3 to the letter.

4.4 The CLH report contains a comparison of the available information with the CLP criteria	**Yes** ☒	**No** ☐

Required information/revisions: None

Recommended information/revisions:
In Section 4.9.5 "Comparison with criteria" (for carcinogenicity), concerning Category 1A, it is suggested that reference in the assessment be made to the fact that this category is for substances that are "known to have carcinogenic potential for humans".

Concerning the assessment for classification as Carc. 1B, please note that the criteria in the CLP Regulation (as quoted in the CLH report) also state that "*In addition, on a case-by-case basis, scientific judgement may warrant a decision of presumed human carcinogenicity derived from studies showing limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals.*" It is suggested that the applicability (or otherwise) of the data for glyphosate in relation to this criterion be also discussed in this section.

Also, please consider whether some of the important factors which may be taken into consideration, when assessing the overall level of concern (CLP Annex I, Section 3.6.2.2.6) should be referred to in the assessment.

4.5 The CLH report provides a justification for using data from a	**Yes**	**No**	**N/A**

different substance	☐	☐	☒

Required information/revisions: None

Recommended information/revisions: None

4.6 The proposal is limited to CMR and/or Respiratory Sensitization hazard classes (Art. 36(1) CLP)	**Yes** ☐	**No** ☒	
4.7 There is a justification for action at EU level presented for other hazard classes than CMR or Respiratory Sensitization (Art. 36(3) CLP)	**Yes** ☒	**No** ☐	**N/A** ☐

Required information/revisions: None

Recommended information/revisions:
Glyphosate has an existing entry in Annex VI to CLP. Normally, in such cases, hazard classes other than CMR-RS where no change is proposed are not addressed in the CLH report and are not open for comment at public consultation (CARACAL paper CA/17/2013 and the follow-up RCOM from Sept 2013).

It is noted that in the CLH report for glyphosate, new data for hazard classes other than CMR-RS where no change is proposed actually are addressed in the CLH report and since the DS has provided an appropriate information basis, assessment and conclusion for these hazard classes, it is assumed that these would be open for comment during public consultation. Please confirm that all hazard classes (human health and the environment), with the exception of respiratory sensitisation, aspiration hazard or hazardous to the ozone layer will be opened for public consultation.

4.8 The CLH report contains confidential information	**Yes** ☐	**No** ☒	
4.9 Confidential information is clearly defined and reported in a separate confidential annex	**Yes** ☒	**No** ☐	**N/A** ☐

Required information/revisions: None

Recommended information/revisions: None

4.10 Other comments on the CLH report

Recommended information/revisions:

The CLH report contains a number of references to documents which all presumably refer to the non-confidential RAR attached in section 13 of the dossier. These include references to Volumes 1 and 3 of the revised Renewal Assessment Report (RAR) dated 31 March 2015 and a reference to .."addendum to the RAR or to the RAR, that are both attached to this CLH report". Furthermore, "addendum on carcinogenicity" and simply "addendum" are also referred to in the CLH report. The CLH report also refers to an "attached EFSA conclusion". In Section 8

Annex 1: Accordance check report for glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

"Annexes", the only relevant annex listed is the "Final Addendum to the Renewal Assessment Report on Glyphosate". Please list these addenda in Section 8 of the CLH report and where necessary, revise the references to these documents in the CLH report.

ECHA would obviously wish to include all these attachments (with the exception of the confidential annex) in the public consultation on the CLH report. Please confirm that this is acceptable to BaUA.

In addition, please note that the header to the annex to the CLH report contains the following text "Glyphosate – Annex Error! Use the Home tab to apply Überschrift 1 to the text that you want to appear here: Error! Use the Home tab to apply Überschrift 1 to the text that you want to appear here."

It may be beneficial to make clear in the report that there are other (confidential) impurities associated with the substance and that at their current concentrations none of these impurities impact the classification of glyphosate.

In addition, please see the comments in the tracked changes version of the CLH report (attached). Where issues have been identified for consideration, please attend to similar issues elsewhere in the CLH report (even if not specifically noted in the suggestions).

5. IUCLID technical dossier

5.1 IUCLID section 2.1 provides information on the classification, according to CLP	**Yes** ☐	**No** ☒

Required information:
The pictogram GHS08 needs to be added to the IUCLID file under "labelling" under the tab "proposed entry".

Recommended information/revisions: None

5.2 The IUCLID dossier contains information flagged as confidential	**Yes** ☒	**No** ☐	
5.3 Confidentiality claims in the IUCLID dossier and in the CLH report are consistent	**Yes** ☒	**No** ☐	**N/A** ☐
5.4 Confidentiality claims in the IUCLID dossier are in accordance with Art. 119 of REACH	**Yes** ☒	**No** ☐	**N/A** ☐

Required information: None

Recommended information/revisions: None

5.5 Other comments on the IUCLID dossier

Recommended information/revisions:
Please ensure that the information on impurities in the confidential annex and the IUCLID file are consistent.

Annex 2: Classification table - Accordance check of glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

Dossier submitter:	Germany
Date of submission:	17/03/2016
Proposed International Chemical Identifier	glyphosate (ISO); N-(phosphonomethyl)glycine
(Proposed) CLP Index Number	607-315-00-8

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

Existing Annex VI entry (CLP, Table 3.1)

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	607-315-00-8	glyphosate (ISO); N-(phosphonomethyl)glycine	213-997-4	1071-83-6	Eye Dam. 1 Aquatic Chronic 2	H318 H411	GHS09 GHS05 Dgr	H318 H411	-	-	-
Dossier submitters proposal	607-315-00-8	glyphosate (ISO); N-(phosphonomethyl)glycine	213-997-4	1071-83-6	**Retain** Eye Dam. 1 Aquatic Chronic 2 **Add** STOT RE 2	**Retain** H318 H411 **Add** H373	**Retain** GHS09 GHS05 Dgr **Add** GHS08	**Retain** H318 H411 **Add** H373	-	-	-
RAC opinion	607-315-00-8	glyphosate (ISO); N-(phosphonomethyl)glycine	213-997-4	1071-83-6	Resulting classification	Resulting codes	Resulting labelling pictograms & words	Resulting labelling codes	Resulting labelling suppl. codes	Resulting SCL and/or M factors	Resulting notes or "-"
Resulting Annex VI entry if agreed by COM	607-315-00-8	glyphosate (ISO); N-(phosphonomethyl)glycine	213-997-4	1071-83-6	Resulting classification	Resulting codes	Resulting labelling pictograms & words	Resulting labelling codes	Resulting labelling suppl. codes	Resulting SCL and/or M factors	Resulting notes or "-"

RAC Rapporteurs' observations on the dossier proposing harmonised classification and labelling (CLH) of glyphosate (ISO); N-(phosphonomethyl)glycine

glyphosate (ISO); N-(phosphonomethyl)glycine	
Type:	Active substance in Plant Protection Products under the Annex I Renewal (AIR) process (Regulation (EC) No. 1141/2010 or Regulation (EC) No.844/2012)
ECHA Secretariat	
Scientific Dossier Manager(s):	[redacted]
Email of dossier manager:	[redacted]@echa.europa.eu [redacted]@echa.europa.eu
Contact point RAC Secretariat:	[redacted]
Email of the contact point:	[redacted]@echa.europa.eu
Rapporteurs appointed by RAC:	[redacted] Additional *ad hoc* WG members: [redacted]
Rapporteurs comments completed:	25 April 2016

1. Health hazards

4.7 STOT RE

A classification of Glyphosate as STOT RE 2 is proposed in the CLH report based on an increase in maternal deaths in the rabbit developmental toxicity studies. In the assessment for a classification as STOT RE 2 it would be appreciated if the day the animals die were included in the CLH report and not only in the DAR since this information is considered relevant for a decision on a classification for STOT RE. This is to make it possible to distinguish between an acute effect e.g. if the death occur within a very few days after start of dosing, or if the death is related to a classification as STOT e.g. if the death occur following several days of dosing. When looking into the DAR the gestational day at which the rabbits die is included and should therefore also be included in the CLH report.

Annex 3: RAC Rapporteurs' observations on glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

4.9 Carcinogenicity

4.9.1 Non-human information
In table 24 of the CLH report in the column describing "Targets/effects" arrows indicate if the effects increase or decrease, however, there are no information regarding if the effect are statistically significant or not. Such information would be helpful in the assessment of the studies.

In this section just before the description of the "Islet cell tumours" please add an explanation regarding how and why the reported incidences were re-evaluated by the DS (e.g the statistic tools used).

The "Islet cell tumours" could better be described as "Pancreatic Islet cell tumours".

The information in the CLH report regarding Historical Control Data (HCD) for the various tumour types reported in the experimental animal studies should be considered to be presented in a more focused manner e.g in a table. Further, it should be described if the HCD were in accordance with the requirement described in the CLP Guidance (see section 3.6.2.3.2 (a)).

In the most recent CLH report template (shttp://echa.europa.eu/web/guest/support/guidance-on-reach-and-clp-implementation/formats)
"Table 52: Compilation of factors to be taken into consideration in the hazard assessment" is included and take into account all considerations for a classification for carcinogenicity according to CLP Annex I section 3.6.2.2.4. Such an overview of these factors could be considered included in the CLH report to help in the assessment of carcinogenicity.

Table 41 in the CLH report with the incidences of the three tumour types under discussion in male CD-1 mice are summarised with regard to dose-response. The table is considered to give a quick overview of the studies, however we found it a bit difficult to read, so a suggestion is to put together the various studies and dose-groups separately (e.g AAAA, BBBB...)

Section 4.9.2 Human information
It would be highly appreciated if a summary table of the various epidemiological studies is included in the beginning of this section, including type of epidemiological study and the results.

Section 4.9.3 Other relevant information
The first paragraph in this section should be deleted or rephrased since if relevant data on mode of action is available, this is used in the decision on classification and labelling for carcinogenicity.

Section 4.9.4 Summary and discussion of carcinogenicity
In the first paragraph of this section it is considered that the following part of the sentence marked in cursive should be deleted: "This is an unusual situation for classification and labelling of chemical substances., *and the common criteria of the CLP Regulation may not be applicable directly. Therefore,* All available data were considered together using a weight etc...., since it is considered that the CLP criteria could be used in the assessment of the animal studies.

In the last paragraph of this section the sentence starting with "Epidemiological studies are of limited value for detecting the carcinogenic potential of an active substance since humans are never exposed to single compound alone *"in plant protection products"* should be included after "active substance".

Annex 3: RAC Rapporteurs' observations on glyphosate (ISO); N-(phosphonomethyl)glycine (submission number: EM011055-54)

4.10 Toxicity for reproduction

4.10.1 Effects on fertility

4.10.1.1 Non-human information

In table 42 of the CLH report in the column describing "Targets/Main effects" arrows indicate if the effects increase or decrease, however, there are no information regarding if the effect are statistically significant or not. Such information would have been helpful in the assessment of the studies.

It is described that the study by Suresh, 1993 is performed with too low doses ((0, 10, 100, 1000 and 10000 ppm), however, the study by Moxon, 2000 is also performed with doses up to 10000 ppm (0, 1000, 3000 and 10000 ppm); please explain.

In the study by Reyna, 1990 a reduction in litter size was reported, it would be appreciated if the magnitude of the reduction were reported in the CLH report.

A delay in sexual maturation was reported as a delay in preputial separation in male F1 pups in the study by Dhinsa et al., 2007. It would be appreciated if some information was included in the CLH report regarding the body weight of the F1 male offspring to assess if the delay in sexual maturation was related to a reduction in offspring body weight.

4.10.2 Developmental toxicity

4.10.2.1 Developmental

In table 43 and 44 of the CLH report in the column describing "Targets/Main effects" arrows indicate if the effects increase or decrease, however, there are no information regarding if the effect are statistically significant or not. Such information would be helpful in the assessment of the studies.

4.10.4 Summary and discussion of reproductive toxicity

In the first paragraph of this section it is considered that the following part of the sentence marked in cursive should be deleted: "This is an unusual situation for classification and labelling of chemical substances., *and the common criteria of the CLP Regulation may not be applicable directly. Therefore,* All available data were considered together using a weight etc....since it is considered that the CLP criteria could be used in the assessment of the animal studies. This also applies to the first paragraph in section 4.10.5.2 Developmental toxicity under General remark (above)