Hazard property hp 14 'ecotoxic': correspondence of classification of waste by the european list of waste, by chemical composition and by an ecotoxicological test battery

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HAZARD PROPERTY HP 14 'ECOTOXIC': CORRESPONDENCE OF CLASSIFICATION OF WASTE BY THE EUROPEAN LIST OF WASTE, BY CHEMICAL COMPOSITION AND BY AN ECOTOXICOLOGICAL TEST BATTERY

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SUMMARY: The Member States of the European Union have in 2014 updated the list of waste and defined the 15 hazard properties (HP) of wastes except for HP14 'Ecotoxic'. Four calculation methods for HP 14 are assessed till June 2015 in a Call for Tenders of the Directorate General of the Environment of the European Commission. This paper is a contribution to the assessment of these 4 calculation methods, with the presentation of results of a 5th one, using "extended M-factors". Available data of 33 samples from different origin were used. They were classified by the LoW: 16 hazardous (H), 7 non-hazardous (NH), and 10 mirror entries (H or NH).

The LoW is taken as a reference method. The concordance for one calculation method is established by the number of waste with identical classification by the considered calculation method and the LoW (H/H, NH/NH). The discordance is established as well, and the case where the waste is classified "H" in the LoW and "NH" by calculation (under-estimation of the hazard) will be considered. Method 2 with extensive M-factors (the 5^{th} one) matches best with the European list of waste (78% concordant H and non-H by LoW, and 13% discordant for H waste by LoW). It classifies safely waste containing substances with high ecotoxicity. Methods 1 and 3 have nearly as good matching (74% concordant H and non-H by LoW, and 6% and 13% respectively discordant for H waste by LoW), but do not classify safely waste containing substances with high ecotoxicity. Method 2 with M-factors limited to the M-factors published in the CLP has insufficient concordance (61% concordant H and non-H by LoW, and 50% discordant for H waste by LoW). As the same method with extended M-factors gives the best performance, the lower performance is due to the limitation of the M-factor. Method 4 is divergent (57% concordant H and non-H by LoW, and 56% discordant for H waste by LoW). The results of a European battery of ecotoxicological tests will be presented at the Conference.

1. INTRODUCTION

The Member States of the European Union have in 2014 updated the list of waste (EC 2014a) and defined the 15 hazard properties (HP) of wastes (EC 2014b) except for HP14 ‘Ecotoxic’. This hazard property is the most frequent classifying property for waste (Hennebert et al 2014) if the Classification, Labelling and Packaging of Preparation and Mixtures calculation method (CLP Regulation 2008), limited to two levels of chronic ecotoxicity, but including extended M-factors, is used.

Four calculation methods are assessed till June 2015 in a Call for Tenders of the Directorate General of the Environment of the European Commission (DG ENV 2014). They differ by the hazard statement codes, the concentration limits, and the use of M-factors. The assessment is focused on so-called “mirror entries” in the European List of Waste (LoW), that is waste that can be either hazardous or non-hazardous, and that must be assessed for their hazard properties by chemical composition or by tests.

This paper is a contribution to the assessment of these 4 calculation methods, with the presentation of results of a 5th one, using “extended M-factors”, i.e. M-factors calculated from reviewed EC50 and NOEC of a broader range of mineral and organic substances, including substances important in waste, like polycyclic aromatic carbons (PAH). Using “absolute entries” of the LoW as a reference, the different classification methods by calculation can be ranked for matching with the LoW classification.

The results of a European battery of ecotoxicological tests will be presented at the Conference.

2. MATERIAL AND METHODS

2.1 Calculation methods for HP 14, and justification of a method with extended M-factors

The different calculation methods (named Method 1 to 4) in the Call for Tenders are presented in the right part of Table 4. For each method, each rule of classification is written as a column in the Table. To assess HP 14, each concentration of a substance with the hazard statement code must be divided by concentration limit specified in the table, and the ratios mut be summed. The sum of these ratios is a hazard index. If it is ≥ 1, the waste is hazardous for this rule of classification. If it is <1, the waste is considered as non-hazardous for that rule.

We have used also a fifth method (named Method 2 with extended M-factors). The limitation of hazard assessment to chronic ecotoxicity of level 1 and 2 (not taking into account level 3 of CLP – level 4 is presented as a “safety net” in the CLP) for waste is argued by an impact assessment (Hennebert and Rebishung 2012). Another reason is that there is only one final level of hazard for waste (Hazardous) but there are 4 levels of hazard for products (Ecotoxic acute, Ecotoxic chronic level 1, 2, 3). This method is used in France since 2012.

The LoW is taken in this paper as a reference method. This implies that the wastes used here are classified as hazardous for HP 14 in the LoW. In practice, this can not be established with absolute certainty. The concordance for one calculation method is established by the number of waste with identical classification by the considered calculation method and the LoW (H/H, NH/NH). The discordance is established as well, and the case where the waste is classified “H” in the LoW and “NH” by calculation (under-estimation of the hazard) will be considered.

2.2 Waste and Waste composition data

Thirty three samples from different origin were used (Table 4). They were classified by the LoW: 16 hazardous, 7 non-hazardous, and 10 mirror entries.

Most of the waste have been analysed according to AFNOR XP X30-489 “Determination of elements and substances in waste”. That method is discussed as a European standardization Work Item submitted to formal vote (CEN/TC 292 2015). The method gives a full knowledge of the waste to be characterized and classified. The results can be used for waste hazard classification, Seveso classification, Water Framework Directive classification, transport regulation, and occupational health and safety requirements. Please be aware that hazard classification with uncomplete analytical data is misleading.

The analytical mass balances (sum of all measured concentrations) were > 90%. Some of these wastes have been presented in Hennebert et al. (2013). When a concentration of a substance is below its limit of quantification (LOQ), the LOQ has been used as the concentration. The concentrations are expressed on dry matter for solid waste and on raw mass (including water) for liquid waste. The hazard indexes can be expressed on dry matter or on raw mass by simple conversion with the moisture content.

2.3 Speciation of mineral elements to mineral substances

Classification by chemical composition depends in waste on hypothesis of speciation of elemental concentrations into mineral chemical substances. The chemical classification is hampered in routine by this question. Where the CLP is mainly focused on chemicals and formulations consisting of pure substances and mixtures of pure substances, the waste regulation covers a wide range of materials which are poorly defined in terms of the chemical form of the substances they contain. Lack of information on the chemical form of substances (speciation) could lead to the use of “worst case” hypothesis, a poor surrogate for hazardousness, and a possible delisting as hazardous (Hennebert and Weltens 2014). A presentation of the different available methods with a step-wise method (depending on the concentration of the element) can be found in AFNOR FD X30-494 (2015) and in an Annex of Hennebert and Rebishung (2015).

A first step to avoid expensive speciation work is to use “worst case with information” calculations, i.e. to suppose that the element is in the most hazardous form in the waste, and that can realistically be present in the waste. “Simple” substances with one ecotoxic element are used rather than more complex substances (i.e. sodium chromate instead of lead chromate). List of such substances can be found for all HPs in Hennebert and Rebischung (2015).

2.4 M-factors

In the CLP, multiplying factors of the concentrations of the substances that produce biological effects in tests at concentration < 1 mg/L are used to calculate the hazard for aquatic environment. The Table 3.1 of Annex VI of the CLP has a (restricted) list of M-factors. The M-factors should be calculated for each substance for acute toxicity (depending on the concentration having 50% of biological effect EC50 if < 1 mg/L, < 0.1 mg/L, < 0.01 mg/L, …) and for chronic ecotoxicity (depending on the concentration with no observed effect NOEC if < 0.1 mg/L, < 0.01 mg/L, < 0.001 mg/L, …) (CLP 2008 ATP 02). Tables of M-factors can be found in Hennebert and Rebischung (2013, updated in 2015).

2.5 European battery of ecotoxicological tests

An aquatic and terrestrial tests battery (Table 1) is proposed by the Ministry for Ecology, France, from a proposal of J. Römbke, ECT (Germany) and P. Pandard, INERIS (France) (2013), and from a previous proposal of the consulting company Ökopoll (2008). The test battery can be operated stepwise, and stopped in one test result is lower than its proposed concentration limits.

The design of the toxicity tests follows a dilution approach, meaning that the waste (eluate or solid) is mixed with a control substrate (e.g. culture medium of reconstituted water or artificial soil). The results of these tests can be expressed as EC_x values (concentration of eluate or solid in the mixture with the control substrate producing an effect of x %) or as LID values (= lowest ineffective dilution rate). If one of the EC values in the eluate tests is below a specific limit value (or one of the LID values is above a specific limit value), the waste is classified as hazardous. Otherwise, solid waste tests are carried out. The waste is considered as non-hazardous only if the results of all tests are above the concentration limits.

It is accepted in substance classification for toxicology and ecotoxicology that results of tests overwhelm results of calculations. If the classification by calculation is dubious (by lack of information), then the test battery should be performed.

At the time of writing, all the ecotox results are not available. Full results will be presented at the conference. Many different test battery can be proposed. We think that, more than the choice of the test composing the battery, the crucial point is to establish concentration limits that match with the Low classification. The results will be presented at the conference.

Table 1. Proposed test battery and concentration limits for assessing HP 14

Test	*Endpoints*	*EC or LID limit values: the waste is HP 14 if*	*Duration*	*Standard*
Aquatic tests				
Inhibition of the light emission of Vibrio fischeri (Luminescent bacteria test)	Eluate concentration which results in 50% inhibition of light emission (EC50), or Dilution step at which light emission is inhibited by more than 20% in comparison to the control	EC50 ≤ 10% LID > 8	30 min	EN ISO 11348-3(2007)
Freshwater algal growth inhibition test with Desmodesmus subspicatus or Pseudokirchneriella subcapitata	Eluate concentration which results in 50% inhibition of population growth (EC50), or Dilution step at which population growth is inhibited by more than 25% in comparison to the control	EC50 ≤ 10% LID > 8	72 h	EN ISO 8692 (2012)
Inhibition of the mobility of Daphnia magna -	Eluate concentration which results in 50% inhibition of mobility (EC50), or Dilution step at which mobility is inhibited by more than 20% in comparison to the control	EC50 ≤ 10% LID > 8	48 h	EN ISO 6341 (2012)
Terrestrial tests				
Soil contact test with Arthrobacter globiformis (bacteria contact test)	Waste concentration which results in 50% inhibition of enzyme activity (EC50), or Dilution step at which enzyme activity is inhibited by more than 30%	EC50 ≤ 10% LID > 8	6 h	ISO/DIS 10871 (2008)
Effects of chemicals on the emergence and growth of higher plants (Avena sativa, Brassica napus)	Waste concentration which results in 50% inhibition of growth (EC50), or Dilution step at which growth is inhibited by more than 30%	EC50 ≤ 10% LID > 8	14 d	ISO 11269-2 (2012)
Avoidance test with earthworms (Eisenia andrei/fetida)	Waste concentration which affects behaviour by 50% (EC50), or Dilution step at which behaviour is impacted by more than 40%	EC50 ≤ 10% LID > 8	48 h	ISO 17512-1 (2007)

LID : lowest ineffective dilution

3. 2. ARITHMETIC COMPARISON OF THE CALCULATION METHODS FOR HP 14

To give an insight about the proposition of DG ENV and the proposition of a fifth method, the five calculation methods can temptatively be classified by increasing concentration limit, taking into account the following observations:

a. A waste classified for acute ecotoxicity is always classified for chronic ecotoxic (empirical results not shown for this set of data, other data in Hennebert et al. 2014). The reverse is not true. That statement could not be verified if the waste contains hazardous degradable substances that can have a acute M-factor greater than a chronic M-factor. This is i.e. the case for some PAH: benzo[k]fluoranthene, M_{acute} = 100, $M_{chronic}$ = 10; anthracene, 100 and 10 respectively; fluoranthene, 100 and 10; pyrene, 10 and 10; phenanthrene, 10 and 1). Excepted for these cases, the comparison of methods may therefore be limited to chronic ecotoxicity;

b. References to hazard statement code (HSC) H412 and H413 do not play a practical role in the classification of waste, because the cumulative concentrations must achieve 25% and such concentrations are unlikely to be present in the waste. The substances with these hazard statements codes (H412: 431 substances, and H431: 254 substances) in Table 3.1 of Annex VI CLP are mainly for H412 synthetic organic chemicals, and the minerals tin chloride and powdered nickel (excluding rare substances), and for H413 elements and substances containing Ni, Co, Se, U, Tl and cadmium sulfide. With 25% cumulative concentration, these materials will not be *a priori* material that the holder wishes to discard, but rather a resource which he will seek to use due to their technical or commercial value. Comparing methods can therefore be confined to the limits of concentration of H410 and H411 substances;

c. The arithmetic ranking concentration limits of the 5 calculation methods for chronic ecotoxicity H410 and H411 depends on the value of chronic M-factor.

If a mean chronic M is hypothetized, a classification by increasing concentration limit can be set (Table 2). The exact classification will depend on the presence of substances with chronic M-factor > 10. The rank of Methods 2 and 4 can in that case move forward.

Table 2. Arithmetic comparison of 5 classification methods for HP 14 by calculation (hypothesis that mean chronic M-factor = 10) (concentration limits for H410 and H411 substances).

Method 3	Method 1	Method 2 with ext. M-factors ($M_{chronic}$=10)	Method 2 with CLP M-factors ($M_{chronic}$=10)	Method 4 ($M_{chronic}$=10)
0.1%	0.25% + 2.5%	2.5/M% + 25%	2.5/M% + 25%	2.5/M% or 25%

4. RESULTS AND DISCUSSION

The 33 results are presented at Table 3, ordered by method with decreasing matching with the Low. The correspondence score are presented at Table 4, and a synthesis at Table 5.

Table 3. Classification of the classification of 33 wastes by the European list of waste (LoW) and by 5 calculation methods (H = hazardous, NH = non-Hazardous, M = mirror entry of the LoW)

N	Waste	LoW	LoW	M3	M1	M2 +ext. M	M2	M4
13	Municipal Solid Waste Incinerator (MSWI) fly ash	19 01 05*	H	H	H	H	H	H
14	Air Pollution Control (APC) residue industrial waste #1	19 01 07*	H	H	H	H	H	H
16	Industrial waste bottom ash	19 01 11*	H	H	H	H	H	H
19	Packages and materials #2	19 12 11*	H	H	H	H	H	H
28	Hydrocarbon #1	13 07 03*	H	H	H	H	H	H
58	Sulfidic acid mine residue Pb Zn Cd	01 03 04*	H	H	H	H	H	H
67	MSWI APC 3	19 01 07*	H	H	H	H	H	H
59	APC residue from animal meal incineration	19 01 07*	H	H	H	H	H	NH
10	Wastes from transport tank cleaning, mixed sludge of food and chemical transport	16 07 09*	H	H	H	H	NH	NH
11	MSWI Air pollution control (APC) residue, bicarbonate process	19 01 07*	H	H	H	H	NH	NH
12	MSWI APC residue, lime process	19 01 07*	H	H	H	H	NH	NH
43	APC residue from municipal waste after solid fuel, metals and organic matter separation	19 01 07*	H	H	H	H	NH	NH
63	Treated wood containing hazardous substances	17 02 04*	H	H	H	H	NH	NH
66	Acid-generating tailings from processing of sulphide ore	01 03 04*	H	H	H	H	NH	NH
17	Metallic dust from aluminum industry	10 03 19 *	H	H	NH	NH	NH	NH
64	Waste from physical and chemical processing of metalliferous minerals Cu Zn	01 03 07*	H	NH	NH	NH	NH	NH
46	Bauxite residue	01 03 09	NH	NH	NH	NH	NH	NH
57	Demolition concrete 2	17 01 01	NH	NH	NH	NH	NH	NH
8	Sludges from treatment of urban waste water	19 08 05	NH	H	NH	NH	NH	NH
5	Non-composted organic fraction of municipal wastes < 30 mm after crushing,	19 05 01	NH	H	H	NH	NH	NH
62	Composted sewage sludge	product	NH	H	H	H	NH	NH
68	Ferrous metal dust and particles	12 01 02	NH	H	H	H	NH	NH
65	End-of-life tyres, crushed 4 mm	16 01 03	NH	H	H	H	H	H
44	Surface treatement - sludges and filter cakes	11 01 09* or 11 01 10	M	H	H	H	H	H
45	Bottom ash and slag from municipal waste after solid fuel, metals and organic matter separation - maturated and pretreated	19 01 11* or 19 01 12	M	H	H	H	H	H
61	Boiler dust from animal meal incineration	19 01 11* or 19 01 12	M	H	H	H	H	NH
3	Mixed municipal waste, fraction > 30 mm after crushing	19 05 01 or 20 03 01	M	H	H	H	NH	NH
4	Compost from mixed municipal waste, fraction < 30 mm after crushing	19 05 01 or 20 03 01	M	H	NH	NH	NH	NH
60	Bottom ash from animal meal incineration	19 01 11* or 19 01 12	M	H	NH	NH	NH	NH
1	Municipal waste - Organic fraction separately collected	20 01 08 or 20 02 01	M	NH	NH	NH	NH	NH

6	Active landfill leachate containing hazardous substances or landfill leachate other than those mentioned in 19 07 02	19 07 02* or 19 07 03	M	NH	NH	NH	NH	NH
7	Closed landfill leachate containing hazardous substances or landfill leachate other than those mentioned in 19 07 02	19 07 02* or 19 07 03	M	NH	NH	NH	NH	NH
9	Sludges from landfill leachate, after evapo-concentration	19 02 05* or 19 02 06	M	NH	NH	NH	NH	NH

Table 4. Comparison of the classification of 33 wastes by the European list of waste and by 5 calculation methods, and calculation methods (H = hazardous, NH = non-Hazardous, M = mirror entry of the LoW)

HP 14 Calculation Methods						Hazardous or Non Hazardous or Mirror entry by LoW	H or NH by method		Matching classification (23 samples)	Calculated NH but H by LoW (16 samples)
Method 3						LoW \ Method 3	H	NH	17	2
∑	Acute	Chronic				H	15	1	74%	6%
H400						NH	5	2		
H410		0.10%				M	6	4		
H411			2.50%							
H412				25%						
H413					25%					
Method 1						LoW \ Method 1	H	NH	17	3
∑	Acute	Chronic				H	14	2	74%	13%
H400	25%					NH	4	3		
H410		0.25%	25%			M	4	6		
H411		2.50%	25%							
H412		25%	25%							
H413			25%							
Method 2						LoW \ M2 + ext. M-factors	H	NH	18	3
∑	Acute	Chronic				H	14	2	78%	13%
H400	$25/M_{acute}$ %					NH	3	4		
H410		$2.5/M_{chronic}$ %				M	4	6		
H411		25%								
H412						LoW \ Method 2	H	NH	14	9
H413						H	8	8	61%	50%
						NH	1	6		
						M	3	7		
Method 4						LoW \ Method 4	H	NH	13	10
∑	Acute	Chronic				H	7	9	57%	56%
H400						NH	1	6		
H410		$2.5/M_{chronic}$ %				M	2	8		
H411			25%							
H412										
H413										

Table 5. Concordance of methods (synthesis)

Method	M2 with extended M-factors	M3	M1	M2 with CLP M-factors	M4
Matching with LoW (H/H, NH/NH)	78%	74%	74%	61%	57%
Mismatching : H by LOW and NH by calculation	13%	6%	13%	50%	56%

The methods rank differently with the LoW.

Method 2 with extended M-factors is the most concordant, and the second (with Method 1) in rank of mismatching.

The other calculation methods then rank in the order of concentration limits set forth above, with decreasing performance.

Methods 3 and 1 have a good agreement with the LoW. They have low concentration limits (method 3: 0.1%; Method 1: 0.25%) but do not classify correctly in relation to the LoW waste containing substances with high chronic M-factors (> 10):

- Mineral substances: compounds of Hg and Cd (chronic M = 100)
- Organic substances: PAHs and pesticides (chronic M = 100 to > 1000).

The wastes that may contain these substances are wastes of the chemical or metallurgical industry, petroleum products and combustion residues, pesticides packaging, and soils, sludges and contaminated sediments. Some tested wastes contain PAHs, which explains the differences in ranking.

In this set of waste, there is a PAH, benz(a)anthracene in sample 28, and a pesticide, chlorpyrifos, in sample 19.

Method 2 with M-factors of CLP provides a lower ranking correspondence. As the same method with extended M-factors gives the best performance, the lower performance of this method clearly comes from the limitation of the M-factor.

Method 4 is little concordant or even divergent.

5. CONCLUSIONS

The methods can be ranked by concordance with the LoW:

Method 2 with extensive M-factors:

- matches best with the European list of waste (78% concordant H and non-H by LoW, and 13% discordant for H waste by LoW);
- classifies safely waste containing cadmium, mercury (chronic M-factors = 100), polycyclic aromatic hydrocarbons – PAHs (frequently M_{acute} = 100, $M_{chronic}$ = 10), pesticides (frequently M_{acute} and $M_{chronic}$ = 1000 or 100) and in general the substances with high ecotoxicity).

Methods 1 and 3 have nearly as good matching (74% concordant H and non-H by LoW, and 6% and 13% respectively discordant for H waste by LoW), but do not classify safely waste containing substances with high ecotoxicity.

Method 2 with M-factors limited to the M-factors published in the CLP has insufficient concordance (61% concordant H and non-H by LoW, and 50% discordant for H waste by LoW). As the same method with extended M-factors gives the best performance, the lower performance is due to the limitation of the M-factor.

Method 4 is divergent (57% concordant H and non-H by LoW, and 56% discordant for H waste by LoW).

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REFERENCES

AFNOR 2015. FD X30-494. Fascicule de documentation. Caractérisation des déchets - Speciation des éléments dans les déchets. 18 p. www.afnor.org

Annex 3.1 of CLP version ATP02, Joint Research Centre of the EU, http://ecb.jrc.ec.europa.eu/classificationlabelling/ clp/ghs/downanx6.php, Excel® file version).

CEN/TC292. 2015. CEN/TC 292/WG 5 N 735 Determination of content of elements and substances in waste - experimental AFNOR Standard XP X30-489 (CEN/TC 292 N 1430)

CLP Regulation 2008. Classification, Labelling and Packaging of Substances and Mixtures Regulation (CLP). 1350 pp.

DG ENV 2014. "Call for tenders ENV.A.2/ETU/2014/0023r - Study to assess the impacts of different classification approaches for hazard property "H 14" on selected waste streams", May, 2014.

EC 2014a. Commission Decision 2014/955/EU of 18 December 2014 amending Decision 2000/532/EC on the list of waste pursuant to Directive 2008/98/EC of the European Parliament and of the Council. http://eur-lex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:32014D0955&rid=1

EC 2014b. Commission Regulation (EU) No 1357/2014 of 18 December 2014 replacing Annex III to Directive 2008/98/EC of the European Parliament and of the Council on waste and repealing certain Directives. Official Journal of the European Union. 19.12.2014. L 365/89.

Hennebert P, Rebischung F. 2012. Classification of industrial waste for hazard properties HP4, HP6, HP8, HP13 and HP14 criteria based on substance concentrations, and impact assessment of options for HP14 on classification of various wastes, composts, sediments and soils. Technical Report INERIS DRC-12-125740-03014A. 10/03/2012. 104 p.

Hennebert P, Rebischung F. 2013. Waste Hazardousness Assessment - Proposition of methods. Report INERIS- DRC-13-136159-04172A- 69 pp. http://www.ineris.fr/centredoc/drc-13-136159-04172a-hazardous-waste-assessment-f3-1379929842.pdf

Hennebert P, Rebischung F. 2015. Waste Hazardousness Assessment - Proposition of methods version 2. Report INERIS- DRC-15-149793-04619A- 102 pp. Available upon request.

Hennebert P, van der Sloot H, Rebischung F, Weltens R, Geert L, Jhelmar O. 2014. Classification of waste for hazard properties according to the recent propositions of the EC using different methods. Waste Management 34 (2014) 1739–1751. PII: S0956-053X(14)00247-5, DOI: 10.1016/j.wasman.2014.05.021

Hennebert P, Weltens R. 2014. Special Session: developments in hazard property classification and methods. Proceedings of 4th International Conference on Industrial and hazardous Waste Management, Chania (Greece), 2-5/09/2014. 10 pp.

Ökopol 2008. Review of the European List of Waste, Final Report, Nov 2008. 532 pp.

Pandard P, Römbke J. 2013. Proposal for a "Harmonized" Strategy for the Assessment of the HP 14 Property. Integr Environ Assess Manag. 2013 Oct; 9(4):665-72.