Hygiene-related assessment of "non-relevant" metabolites (as defined in chemicals law) of active substances of plant protection products in drinking water[1]

Recommendation of the German Federal Environment Agency (UBA) after hearing the Drinking Water Commission of the Federal Ministry of Health at the UBA

A. Summary: Essence and addressees of this recommendation

This recommendation is directed at

1. the public authorities responsible for monitoring drinking water and
2. water suppliers.

It also provides information

1. to manufacturers of plant protection products (PPPs) and
2. authorities responsible for the authorization of PPPs in accordance with the German Plant Protection Act (*Pflanzenschutzgesetz - PflSchG*).

The recommendation is intended to impart the technical basis for voluntary co-operation between stakeholders (cf. Section E) in the field of "protection of raw and drinking water" concerning such degradation products of active substances of PPPs as are defined as non-relevant in EU chemicals law.[2]

Co-operation of the kind mentioned above is aimed at implementation of Article 6 (3) of the German Drinking Water Ordinance (*Trinkwasserverordnung – TrinkwV 2001*) – "minimization order" – for the purpose of keeping raw water or groundwater intended for the production of drinking water as free as possible of non-relevant metabolites, without legally binding standards. This co-operation commences at the "source" of contamination (cf. recital 28, Drinking Water Directive 98/83/EG). An important means of realization of the minimization order in this connection is the legally-binding designation of water protection areas.

The Drinking Water Commission of the German Federal Ministry of Health at the Federal Environment Agency (UBA) proposed in 2006 that a clear conceptual distinction be made in the regulative area of drinking water between "non-relevant" metabolites – described as "relevant contaminants" – and relevant metabolites [1].

Pursuant to the present recommendation, for the time being only those non-relevant metabolites that can be expected or are measured in drinking water above concentration(s) defined in the recommendation are also relevant contaminants of drinking water (from agricultural applications). Depending on legal or technical context (Plant Protection Act or drinking water

[1] Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz 2008 • 51:797-801 (in German). Online release 04.04.2008: http://www.springerlink.com/content/21n1042mv8327820/fulltext.pdf.

[2] According to Drinking Water Directive 98/83/EEC they also belong to "relevant metabolites, degradation and reaction products (of active substances of PPPs), however not to such simple degradation products as CO_2, sulphate, H_2O etc., since their development *cannot* be attributed in a specific case to a particular active substance, and from that point of view can also not "correspond" structurally to such an active substance.

hygiene), they are described hereafter as non-relevant metabolites or relevant contaminants.

The Drinking Water Ordinance of 2001 lays down no limit values for non-relevant metabolites. Nevertheless, depending on water solubility/polarity, sorbability and persistence, non-relevant metabolites can penetrate into raw water used or intended for the production of drinking water as relevant contaminants, as in the case of other physiochemically-comparable environmental contaminants in the course of virtually natural processes of water treatment.[3] As such, they are regarded by water suppliers, without further consideration of effect criteria, as potentially "relevant to drinking water".

The presence or accumulation of non-relevant metabolites in the water cycle endangers the quality of drinking water in the long term, and is therefore undesirable on the grounds of drinking water hygiene.[4] In the case of oxidative water treatment, they may become, as in the case of relevant contaminants of another source, the reactive starting point of toxicologically relevant transformation products.

The UBA therefore proposes, after hearing the Drinking Water Commission, two health-related indication values (HRIV) and one precautionary action value (PAV)[5] as a basis for assessing non-relevant metabolites as relevant contaminants of drinking water:

- The alternatives $HRIV_a$ or $HRIV_b$ of 1.0 or 3.0 µg/l, respectively, stem from the UBA recommendation of March 2003 [2] on the assessment of the presence of substances that are not assessable from a health point of view. They are lifelong acceptable for the time being on a permanent basis, pending possible legislation, as a maximum value for non-relevant metabolites or totals thereof. Which of the two values should be applied in a specific case depends on the quality of the toxicological database of the non-relevant metabolite(s) concerned. In justified isolated cases, the proposed $HRIV_a$ or $HRIV_b$ for a specific case can be adjusted upwards.
- The PAV of 10 µg/l for a non-relevant metabolite stems from the EU Guidance Document [3][6]. According to this recommendation, it is only temporarily acceptable until reattainment of or lower deviation from the HRIV for the respective substance (group). The PAV is based in this respect on the UBA recommendation on "action values for substances in drinking water applicable during periods of limit value exceedance (…)" of August 2003 [4].

After hearing the Drinking Water Commission, the Federal Environment Agency recommends the use of one of the above-mentioned values, depending on the level of the measurement value, as an initial basis for the decision on possible control action. This includes, above all, voluntary co-operative measures in water-supply catchment areas and, in particular, water protection areas whose raw water is contaminated with non-relevant metabolites of active substances of PPPs.

Pursuant to Article 6 (2) of the Drinking Water Ordinance of 2001, two legally-binding limit values apply for active substances and their relevant metabolites.

[3] In the opinion of the Drinking Water Commission (meeting of 10.12.2007) such processes are soil passage, slow and rapid sand filtration and cascade aeration, but not filtration by way of activated carbon.
[4] Cf. Communication of the Commission of 02.02.2000 on application of the precautionary principle, COM 2000(1), Introduction (3): "The dimension of the precautionary principle goes beyond the problems associated with a short- or medium-term approach to risks. It also concerns the longer run and the well-being of future generations."
[5] In German: HRIV = Gesundheitlicher Orientierungswert (GOW); PAV = Vorsorge-Maßnahmewert (VMW).
[6] SANCO/221/2000-rev.10, 25.02.2003: Guidance Document on the Assessment of the Relevance of Metabolites in Ground Water of Substances Regulated under Council Directive 91/414/EEC.

B. Legal departure points of this recommendation

1. Differentiation of relevant and non-relevant metabolites of active substances of PPPs.

Degradation products of active substances of authorized PPPs, which,

- with regard to their pesticide activity, have properties comparable to those of the active substance, or which,
- due to their biological efficacy (toxic or ecotoxic properties), endanger groundwater or
- endanger other ecosystems that are dependent on it, or the health of human and animal life,

are subject to the precautionary principle laid down in EU regulations on water and chemicals. A danger to groundwater is presented by such contamination as renders groundwater ineffective in its crucial role for all life processes in the environment, and as provider of the most important basis for the supply of drinking water (Amtsgericht [district court] Braunschweig, 6A 6009/90 and 6A 61195/90 of 12.12.1990, p.18 ff) [5].

The limit value of 0.1 µg/l, which is laid down in Drinking Water Directive 98/83/EC and applicable for groundwater in accordance with Annex VI of Directive 91/414/EEC, has therefore also to be observed in the case of those metabolites that have a pesticide efficacy. The permissibility of a PPP containing the parent compound of such a relevant metabolite is thus dependent on the latter's expected concentration in groundwater not attaining or exceeding the limit value of 0.1 µg/l.

Such degradation products as are of no relevance in the above-mentioned sense in EU legislation on water and chemicals (that is, non-relevant metabolites) are not included in these regulations.

2. The minimization order and prohibition of deterioration in European and German legislation on drinking water

Certain non-relevant metabolites of active substances of PPPs are to be assessed from the point of view of drinking water hygiene as relevant for drinking water due to their great mobility and persistence. EU legislation on water and chemicals does not yet take sufficient account of this perspective.

Pursuant to recital 28 and Article 4 (1) (minimum quality requirements) and Article 4 (2) (prohibition of deterioration) of Drinking Water Directive 98/83/EC, the so-called "minimization order" is implemented in Article 6 (3) of the Drinking Water Ordinance of 2001 as follows: "Concentrations of chemical substances that contaminate water intended for human consumption or can have a negative effect on its quality should (…) be kept as low as possible on the basis of generally accepted rules of technology and reasonable cost, taking account of the circumstances of the respective case."

Against this background, the Drinking Water Commission took a basic stand on 12 December 2006 on the question of the assessment of non-relevant metabolites in drinking water (see [1]), and proposed that non-relevant metabolites,

- whose occurrence in raw and drinking water is observed or expected to be at a level $\geq$ 0.1 µg/l, with corresponding persistence and thus relevance to drinking water, bearing in mind
- the possibility that toxicologically relevant transformation products could arise from non-relevant metabolites during oxidative water treatment,

be described outside the scope of plant protection law as relevant contaminants of raw and drinking water, but assessed from the point of view of drinking water hygiene on the basis of

the limit values for biocidal PPPs contained in the Drinking Water Ordinance of 2001.

Although certain non-relevant metabolites, merely because of their great mobility and persistence, should doubtless be assessed from the point of view of drinking water hygiene as relevant contaminants, the Federal Environment Agency cannot go along with the proposal of the Drinking Water Commission on the quantitative assessment of relevant drinking water contaminants from agricultural sources. Instead, after hearing the Drinking Water Commission, it directs for the time being the following recommendation primarily at the first two addressees mentioned above.

C. Practical departure point of this recommendation

The occurrence of non-relevant metabolites in groundwater intended as raw water for the production of drinking water is not subject to the limit value of 0.1 µg/l applicable for groundwater in accordance with Annex VI of Directive 91/414/EEC. Therefore, non-relevant metabolites can occur as relevant contaminants of raw and drinking water in concentrations that exceed the limit value for biocidal PPPs. In a precautionary step, the Guidance Document (see Footnote 6) therefore recommends a permanently tolerable maximum concentration (standard value) of up to 10 µg/l for all non-relevant metabolites.

Triggered off by findings >10 µg/l of the non-relevant metabolite desphenyl-chloridazone (chloridazone B) and N,N-dimethylsulfamide (DMS[7]) of the active substances chloridazone and tolylfluanide in groundwater in the states of Baden-Württemberg and Bavaria (since mid-2007 also in raw waters in North Rhine Westphalia) intended as raw water for the production of drinking water, the Federal Office of Consumer Protection and Food Safety (BVL) drew up on 11 June 2008 a list of non-relevant metabolites that had been detected in groundwater infiltration analyses in maximum yearly average concentrations in excess of 1 µg/l.

Furthermore, the Water Technology Centre (TZW) of the German Technical and Scientific Association for Gas and Water (DVGW) provided evidence[8] at the end of 2006 – concerning the only recently known DMS, which, due to its intrinsic properties, is assessable as "non-relevant" – that with ozonation of raw water containing DMS under certain circumstances the highly genotoxic and probably human carcinogenic NDMA (N,N-dimethylnitrosamine) arises.

The German Federal Office of Consumer Protection and Food Safety (BVL) therefore ordered, with effect from 19 February 2007, the suspension of authorization of all PPPs that contain the active substance tolylfluanide, their application being permissible only in greenhouses.

D. The recommendation

1. Basis for assessing acceptable relevant contaminants in raw and drinking water

On the one hand, the Drinking Water Ordinance of 2001[9] contains no explicit limit value for non-relevant metabolites of active substances of PPPs. On the other hand, plant protection law assesses the relevance to drinking water (resulting from mobility, water solubility/polarity and persistence) of PPP metabolites from the precautionary point of view merely as a single component of their individual effect potential in groundwater or for human beings. The Plant Protection Act has up to now not provided for their effect-unrelated weighting on the basis of

[7] This is the preferred technical abbreviation for N,N-Dimethylsulfamid, since "DMSA" already stands for dimercaptosuccinic acid as well as for another relevant contaminant of the active substance dichlofluanid.
[8] Letter of the DVGW (German Technical and Scientific Association for Gas and Water) of 24.11.2006 to water utility managements.
[9] Presently being amended.

a solely physiochemically defined "relevance to drinking water". Neither does the Act cover the isolated occurrence of totals of several non-relevant metabolites in drinking water.

The function of non-relevant metabolites as precursor of potential toxicologically-relevant coupled and reaction products of oxidative steps of water treatment has also been of particular interest in recent times.

Article 6 (3) of the Drinking Water Ordinance of 2001 ("minimization order") provides for the possibility of avoiding uncertainties and risks through precautionary action.

After hearing the Drinking Water Commission, the Federal Environment Agency recommends, as a regulatory approach to the, in part, considerable contamination of some raw and drinking waters with non-relevant metabolites or totals thereof, and in order to satisfy the special precautionary demands on drinking water, that the presence of non-relevant metabolites in drinking water be assessed for the time being in the same way as the presence of partly- or non-assessable substances in drinking water.

Contrary to the opinion of the Drinking Water Commission, the Federal Environment Agency does not propose the legally-binding limit values for active substances of PPPs – including biocidal PPPs – contained in the Drinking Water Ordinance of 2001 as an initial basis for assessment. For the time being, the health-related indication values in the UBA recommendation of March 2003 [2] are better suited for this purpose. These are based on the world-wide-accepted TTC concept,[10] and from that point of view they conform to an analogous assessment step [3] in the Guidance Document (see Footnote 6).

The UBA recommendation of March 2003 [2] mentions a permanently tolerable, health-related indication value (HRIV) for all substances, which are not primarily genotoxic, but at the same time cannot be toxicologically assessed on the basis of chronic or subchronic animal experiments, and which show no signs, however, of neurotoxic, immunotoxic or germ-call toxic potential. It has the regulatory function of a precautionary value and, depending on the toxicological assessability of relevant contaminants or totals thereof, is as follows:

a) at most HRIV = 1.0 µg/l[11] and

b) at most HRIV = 3.0 µg/l[12].

Only in isolated cases of the occurrence of non-relevant metabolites in drinking water should there, for the time being, be upward deviation from the proposed HRIV in a specific case in accordance with the UBA recommendation of March 2003. The HRIVs can be applied alternatively, depending on the toxicological assessability of a non-relevant metabolite, and are lifelong acceptable for the time being on a permanent basis, pending possible legislation.

The responsible authority has to decide from case to case on the specific $HRIV_a$ = 1 µg/l or $HRIV_b$ = 3 µg/l, taking into consideration information on the structural and activity relations of the particular non-relevant metabolite, and possibly other non-relevant metabolites, as well as of relevant contaminants from other sources. In most cases, the principle of "similar joint action" of their components and the corresponding addition rule is appropriate for assessment of substance totals.

[10] Management concept of the "threshold of toxicological concern (TTC)", which applies in the case of an incomplete human toxicological database.
[11] ≤ 1 µg/l: The substance is demonstrably not genotoxic. In addition, sound in vitro and in vivo data are available on the oral neurotoxic and germ-cell toxic potential of that substance. This data does not lead to a value that is lower than 0.3 µg/l.
[12] ≤ 3 µg/l: The substance has neither genotoxic nor germ cell toxic nor neurotoxic potential. In addition, sound in vitro and in vivo data are available from at least one study on the subchronic oral toxicity of that substance. This data does not lead to a value that is lower than 1 µg/l.

The UBA department, "Drinking Water and Swimming Pool Water Hygiene", in co-operation with the Federal Institute for Risk Assessment, is available for advice in this connection.

2. Basis for assessing contaminants that are present transiently above a HRIV in raw and drinking water

Should the $HRIV_a$ or $HRIV_b$ be exceeded, which is lifelong acceptable for the time being on a permanent basis pending possible legislation, the UBA recommends that health authorities use a provisionally acceptable PAV as an initial basis for assessment. It can be calculated from the $HRIV_a$ following the interpolation method (that goes back to federal soil protection law) of the UBA recommendation on "action values for substances in drinking water applicable during periods of limit value exceedance (…)" of August 2003 [4].

In this latter recommendation the UBA proposes multiplication of a health-related lifelong tolerable maximum value by a substance-specific, data based interpolation factor IF for derivation of a provisionally tolerable action value for a parameter with limit value according to Article 9 (6) to (8) of the Drinking Water Ordinance of 2001. The level of IF is equivalent to the square root of the product EF_{gh} of all extrapolation factors that, in accordance with the technical commentary [6] on the said recommendation, were used for extrapolation from the respective substance database to human beings.

Extrapolation factors of up to $EF_{gh} = 100$ are applied to extrapolation from secured animal experiment data to human beings. With the resulting $IF = \sqrt{100} = 10$, a provisionally acceptable PAV arises from the $HRIV_a$ for a non-relevant metabolite of the order of

a) $PAV_a = 10$ µg/l.

From the $HRIV_b$ there arises with the same method a

b) $PAV_b = 30$ µg/l.

According to the Guidance Document (see Footnote 6) the following applies however:

c) Long-term exceedance of $PAV_a = 10$ µg/l in groundwater by a non-relevant metabolite has to be avoided / is not provided for.

E. Summary and outlook

1. Summary with table

It follows from Section D1 that, depending on toxicological assessability (a or b) of a non-relevant metabolite, concentrations up to

a) 1.0 µg/l = $HRIV_a$ or

b) 3.0 µg/l = $HRIV_b$

are lifelong acceptable for the time being on a permanent basis, pending possible legislation.

It follows from Section D2 that exceedance of $HRIV_a$ or $HRIV_b$ by a non-relevant metabolite is only provisionally acceptable, and only up to

c) 10 µg/l = PAV.

Table:

Water-hygiene-related, lifelong-acceptable HRIV (from Section D1), for the time being on a permanent basis, pending possible legislation		Water-hygiene-related, provisionally acceptable PAV (from Section D2)
1 µg/l = $HRIV_a$	**3 µg/l = $HRIV_b$**	**10 µg/l = PAV**
Indication value for all non-relevant metabolites, for which essentially no findings are available from subchronic animal experiments (for further information see Footnote 11)	Indication value for all non-relevant metabolites, for which essentially no findings are available from chronic animal experiments (for further information see Footnote 12)	Maximum value pursuant to the Guidance Document (see Footnote 6) and the UBA recommendation on "action values for substances in drinking water applicable during periods of limit value exceedance (see [4]) for all non-relevant metabolites for which a $HRIV_a$ or $HRIV_b$ has been laid down; pursuant to Art. 9 (6) to (8) Drinking Water Ordinance 2001 it applies, however, only provisionally.

2. Outlook for the control of relevant contaminants in drinking water

This recommendation broadens the concept of relevance, as defined in EU chemicals law and implemented in German licensing regulations, to include the relevance to drinking water of a non-relevant metabolite. However, not only non-relevant metabolites of active substances of PPPs have the potential to enter drinking water as relevant contaminants. Environmental contaminants from sources other than agriculture have also to be assessed as relevant to drinking water, before consideration of any effect criteria, when, due to their physiochemical properties, it can be expected that in actual conditions they could enter groundwater that is used or intended to be used for the production of drinking water.

The present recommendation that concentrations of non-relevant metabolites in drinking water be lifelong acceptable (for the time being on a permanent basis, pending possible legislation), and where possible only in values of $HRIV_a$ = 1.0 µg/l or $HRIV_b$ = 3.0 µg/l at the most, and above these levels (up to PAV = 10 µg/l) only provisionally, corresponds to a more stringent approach to water hygiene than can be inferred from the current purely substance-related criteria of EU law on the assessment of the relevance of metabolites of active substances of PPPs.

The UBA therefore expressly welcomes co-operation between primary stakeholders (water suppliers, government surveillance of drinking water) and secondary stakeholders (water pollution control, agriculture and agricultural consultants, manufacturers of PPPs and consumer protection groups), which exists since 1989, or has been established in the meantime in this field of action. Through the introduction of appropriate action, including legal measures, to protect waters that serve the production of drinking water,[13] co-operation of this kind can make an important contribution to reducing contamination of raw and drinking water with non-relevant metabolites to an unavoidable minimum in the medium to long term. Such co-operation reflects the basic principles of integrated plant protection, good agricultural practice and good environmental protection practice when it looks at the reasonableness of the cost and circumstances of the isolated case from both an agricultural and a drinking water hygiene perspective. This includes, in particular, initiatives and agreements on the legally-binding designation of additional water protection areas.

[13] Specified in the statement of the Drinking Water Commission of 12.12.2006, see also [1].

Agricultural co-operation of this kind concurs with the Drinking Water Commission [1], according to which neither relevant metabolites nor so-called "relevant contaminants – as non-relevant metabolites in this recommendation are to be understood – are of benefit to drinking water, where they should therefore basically not be found.

In the present legal situation, control decisions are legally protected that accept, provisionally or permanently, a higher degree of contamination of drinking water with non-relevant metabolites than set out in this recommendation. They appear to be conveyable to the public in those cases where the use of a PPP is unavoidably linked with the existence of one or more non-relevant metabolites at a concentration higher[14] than a HRIV or the PAV proposed in this recommendation. Corresponding control decisions have to be defended and frankly communicated by the responsible parties; they must, however, also remain revisable [5].

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[14] Always, however, as low as possible below purely toxicological derivable values.