DRAWG Opinion on identifying worst-case uses for PT6 biocidal products in order to minimise the number of uses to be assessed for dietary risk
Agreed at TMII13

Background:

At TMIII12, a HEEG Opinion on identifying worst-case operator/user exposure scenarios for PT6 was endorsed; this Opinion aimed at minimising the number of exposure scenarios that have to be assessed for PT6 products, which comprised a very large number of uses.

DRAWG was asked to propose a similar method for identifying the worst-case dietary exposure scenario for PT6 products. This request arose during a specific active substance discussion. For this substance, two dietary exposure scenarios were evaluated in the CAR (consumption of food after contact with cleaned or painted surface and exposure from dishes cleaned with preserved dishwashing detergents). The TM asked for an additional scenario covering the use in paper production where the end product may be used as food packaging. While the CAR for this substance remains unaffected by this Opinion and no additional dietary risk assessment was requested for Annex I inclusion, the TM saw the need for a method aimed at focusing the dietary risk assessment for PT6 products based on worst-case dietary exposure scenarios.

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Summary:

Based on a review of the above mentioned HEEG Opinion and considering the possible dietary exposure scenarios and assessment methods for PT6 biocidal products, this paper uses an example to demonstrate how the worst-case uses for a PT6 product might be determined. Since not all of the worst case dietary exposure scenarios identified in this example may be relevant for any active substance used in PT6, applicants are advised to investigate which of the dietary exposure scenarios need to be addressed for their intended uses within PT6.

Introduction:

As noted in the HEEG Opinion mentioned before, PT6 biocidal products are used to preserve a wide range of products. The range of products identified by HEEG from representative uses in the review programme includes water-basedcoatings, polymer dispersions, filler dispersions, pigment slurries, solutions and dispersions of glues and thickeners, concrete additives, construction materials, detergents, cleaners, textile processing chemicals, paper and leather treatment agents and other aqueous formulations.

Considering these uses, the **dietary exposure scenarios** listed in Table 1 have been identified. Methods for assessing these dietary exposure scenarios can be found in the "TNsG on Estimating Livestock Exposure to Active Substances used in Biocidal Products"[1] (in the following referred to as "Livestock TNsG" as well as in the "TNsG on Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses" and the "TNsG on Estimating Transfer of Biocidal Active Substances into Foods – Non-professional Uses"[2] (in the following referred to as "Food TNsGs". The Food TNsGs have not been finalized. If approaches in the Food TNsGs change, these changes will also apply to this document.

Table 1 Dietary exposure scenarios

Non-professional dietary exposure scenarios (i.e. use in households):
1. Use of PT6 products in dishwashing detergents and subsequent dietary exposure via residues on dishes
2. Use of PT6 products in household cleaners or disinfectants and subsequent dietary exposure via residues on food preparation surfaces
3. Use of PT6 products for in-can preservation of insecticides and subsequent dietary exposure via residues on food preparation surfaces
Professional dietary exposure scenarios:
4. Use of PT6 products for in-can preservation of insecticides and subsequent dietary exposure via residues on food storage/processing surfaces
5. Use of PT6 products in industrial or institutional cleaners or disinfectants and subsequent dietary exposure via residues on food preparation surfaces
6. Use of PT6 products in the production of food contact materials or components thereof, e.g.: ○ paper ○ coatings ○ polymer dispersions
7. Use of PT6 products in production of feed packaging (dietary exposure via transfer of residues from feed packaging to feed, subsequent uptake by livestock animals and resulting deposition in edible animal matrixes): ○ paper ○ coatings ○ polymer dispersions

Methodology for identifying the worst-case use for an example product:

Because many of the parameters influencing the status (worst-case, best-case or in between) of a particular use are variable, it is neither useful nor possible to propose a generic method for identifying the worst-case use/uses. Rather an example has been established in order to demonstrate how the worst-case dietary exposure scenario can be

[1] https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp

[2] Under development

identified for a PT6 biocidal product. In this document, the example PT6 product from the HEEG Opinion (chapter 3) is considered. The conclusions arrived at in this document are valid for this particular example only and will differ for PT6 products with different **use categories** and **combinations of uses**.

The example product is applied in the following **use categories**:

Table 2 Use categories and potential dietary exposure for the example product

Use Category (i.e. field of use envisaged) for the example product	**Likely concentration at which a.s. will be used**	**Potential dietary exposure**
Paints and Coatings – Used to control the growth of bacteria and fungi in water-based paints and coatings in storage containers before use.	7.5 to 30 ppm total a.s.	**Yes - coatings are components of food packaging and components of other food contact materials (e.g. food contact surfaces such as counter tops)**
Liquid Detergents - Used to control the growth of bacteria and fungi in the preservation products such as liquid fabric softeners, dishwashing detergents, liquid laundry detergents, liquid soaps and hand cleaners, and the surfactants used in formulating such products.	6 to 15 ppm total a.s.	**Yes - dishwashing detergents**
Fuel Preservation – Used to control the growth of fungi and bacteria in liquid hydrocarbon fuels and oils, and any associated water bottom phase, including crude oils, aviations fluids, kerosene, heating oils, residual fuel oils, coal slurries, liquefied petroleum gases, petrochemical feed stocks, and diesel fuels.	1.5 to 6 ppm total a.s.	No dietary relevance
Textiles, Leathers and Inks – Used to control the growth of fungi and bacteria in textile (woven and non-woven, natural and synthetic) processing chemicals, inks (lithographic, photographic, ink-jet fluids), and all chemicals used in the leather process industry.	6 to 30 ppm total a.s.	**Yes - inks are components of food packaging**
Polymer Latex Preservation - Used to control the growth of bacteria and fungi in the manufacture, storage, and transport of synthetic and natural polymer lattices and industrial biopolymers.	7.5 to 50 ppm total a.s.	**Yes - polymers form the basis of many types of food packaging and other food contact materials**

Adhesives and Sealants - Used to control the growth of bacteria and fungi in water-soluble and water-dispersed adhesives and tacktifiers in storage containers before use.	7.5 to 30 ppm total a.s.	**Yes - adhesives are components of food packaging**
Mineral Slurries - Used to control the growth of bacteria and fungi in aqueous-based inorganic/mineral slurries and inorganic pigments which are formulated into paints, coatings and paper.	10 to 30 ppm total a.s.	**Yes - formulation into paper used as food or feed packaging; formulation into coatings used in food packaging**
Electro-Deposition Coatings – Used to control the growth of bacteria and fungi in coatings applied by an electro-deposition process and associated rinse systems.	6 to 50 ppm total a.s.	**Yes - coatings are components of food packaging**
Household (HH) and Industrial and Institutional (I&I) – Used to control the growth of bacteria and fungi in products used for car care, floor care, waxes, hard surface cleaners, pre-moistened sponges or mops, and the surfactants used in these types of products.	6 to 25 ppm total a.s.	**Yes - household/industrial/ institutional cleaners (and disinfectants) for food contact surfaces; pre-moistened dish sponges**
Functional Fluids – Used to control the growth of bacteria and fungi in brake and hydraulic fluids, antifreeze, corrosion inhibitors, fuel additives, spinning fluid, and fountain solutions.	6 to 30 ppm total a.s.	No dietary relevance

Methodology for an example product: STEP A

Begin by matching the use categories with dietary relevance from Table 2 with the dietary exposure scenarios from Table 1.

Table 3 Use categories matched with dietary exposure scenarios

Use category	Dietary exposure scenario
Liquid Detergents	scenario 1 (dishwashing)
Household Cleaners/Disinfectants	scenario 2 (household disinfectants)
additional scenario: Household Insecticides	scenario 3 (household insecticides)
additional scenario: Industrial/Institutional Insecticides	scenario 4 (industrial insecticides)
Industrial/Institutional Cleaners/Disinfectants	scenario 5 (industrial disinfectants)
Coatings	scenario 6 (FCM*)
Inks	scenario 6 (FCM*)
Polymer Preservation	scenario 6 (FCM*)
Adhesives	scenario 6 (FCM*)
Mineral Slurries	scenarios 6 (FCM*) and 7 (feed packaging)
* *FCM = food contact materials*	

Methodology for an example product: STEP B

In the next step, predict the worst-case use category within each dietary exposure scenario.

Dietary exposure scenarios 1-3:

As identified in Table 3, the dietary exposure scenarios 1-3 include the following use categories:

- **Liquid detergents** (dietary exposure scenario 1): Use of these products can leave residues on dishes used for serving and eating food. The relevant products are dishwashing detergents and pre-moistened sponges[3].
- **Household Cleaners/Disinfectants** (dietary exposure scenario 2): These products are used to clean food contact surfaces.
- **Household Insecticides** (dietary exposure scenario 3): Aerosols from these products can settle on food contact surfaces.

Food contact with products from these use categories is likely and relatively high because of the large surface area containing residues that is in contact with food, and because use occurs on a daily basis.

For dietary exposure scenarios 1, 2 and 3, dietary exposure is determined via calculation models using default and product-specific values (see Food TNsGs). If the calculations for all

[3] In the HEEG example, these are grouped with hard surface cleaners, but for the purpose of dietary risk assessment, they fit better into the category of liquid detergents

three scenarios result in acceptable exposures (below the ADI/ARfD[4]), no further assessment is required.

According to the Food TNsGs, if the ADI/ARfD values are exceeded, further refinement is required where possible. One possibility is to measure the actual amount of biocide residues on the treated surface and use the measured values in the exposure calculations. Particularly for volatile substances, this amount may be very different from the application rate. Another possibility is the experimental determination of the mass transfer efficiency rate, which can in turn be applied to the exposure calculations [5]. If the refined calculations result in acceptable exposures (below the ADI/ARfD[6]), no further assessment is required.

If studies measuring residues on the treated surface or transfer efficiency rate are performed, generally, it will suffice to conduct these only for the use with the highest exposure value as determined in the calculations. If the resulting exposure estimate is safe (below ADI/ARfD), the same can be assumed for the remaining uses.
However, it must be kept in mind that the formulation of the PT6 biocidal product and the formulation of the product containing the PT6 biocidal product (i.e. the cleaner, disinfectant, insecticide or detergent) influence the release of the PT6 active substance and the residue transfer into food. Particularly in cases where the calculated dietary exposures (before refinement) do not differ much, the formulation might be the discriminating factor. Therefore, if there is an indication that the actual amount of surface residue and/or residue transfer into food will be in different orders of magnitude for the different uses, studies must be performed for all uses. In certain cases, it may be possible to show that the study settings for one use are sufficient to cover the other applications. In such cases, extrapolation of study results might be possible.

Worst case for dietary exposure scenarios 1, 2 and 3: The use with the highest calculated exposure value (only relevant if ADI/ARfD are exceeded)

Dietary exposure scenario 4:

As identified in Table 3, dietary exposure scenario 4 includes the following use category:

- **Industrial/Institutional Insecticides**

According to the Food TNsGs, a dietary risk assessment for industrial/institutional insecticides generally does not have to be performed as long as the insecticide carries appropriate use instructions on its packaging preventing contact with food/food surfaces. Therefore, it is not necessary to determine a worst case. The Food TNsGs further state that there are certain insecticide uses where contact with food surfaces is required. For such uses, the Food TNsGs require residue trials. Therefore, this paper does not apply to such uses.

Worst case for dietary exposure scenario 4: Not applicable.

[4] ADI: Acceptable Daily Intake; ARfD: Acute Reference Dose
[5] Please consult the "Guidance on Estimating Transfer of Biocidal Active Substances into Foods – non-professional uses" (under development) for more information on possible refinement options.
[6] ADI: Acceptable Daily Intake; ARfD: Acute Reference Dose

Dietary exposure scenario 5:

As identified in Table 3, dietary exposure scenario 5 includes the following use category:

- **Industrial/Institutional Cleaners/Disinfectants**

According to the Food TNsGs, for scenario 5, exposure is not calculated using a model calculation. Rather, the results of rinsing/wiping trials are used to determine the need for residue studies[7]. If results are below the threshold levels[8], dietary exposure is considered negligible and no further assessment is needed.

Rinsing/wiping trials will generally only be required for the use with the highest calculated residue per unit area. This can be determined from the a.s. concentrations and the applications rates of the different products (surface cleaners and disinfectants) that contain a PT6 product. If the result of the rinsing trial for the use with the highest calculated residue per unit area is below the threshold levels, the same can be assumed for all other uses in this scenario. However, it must be kept in mind that the formulation of the PT6 product and the formulation of the product containing the PT6 product (i.e. the cleaner or disinfectant) influence the residue transfer into food. Particularly in cases where the residues per unit area do not differ much, the formulation might be the discriminating factor. In this case, rinsing studies might be needed for both uses.

Worst case for dietary exposure scenario 5: The product with the highest residue of a.s. per unit area

Dietary exposure scenario 6:

As identified in Table 3, dietary exposure scenario 6 includes the following use categories:

- **Coatings**
- **Inks**
- **Polymer Preservation**
- **Adhesives**
- **Mineral Slurries**

According to the Food TNsGs, for scenario 6, dietary exposure is calculated using default values (for food intake, body weight and area of contact between the food contact material and the food contained within the food container) as well as the migration rate of the a.s from the food contact material which is determined experimentally for each active substance[9]. Food contact materials present a special case in that they can contain residues of PT6 substances from a variety of sources (e.g. from inks and adhesives; mineral slurries formulated into packaging paper; coatings; polymer dispersions made into plastic

[7] Please note that this is the current proposal in the Food TNsG which has not been finalised. If the approach in the Food TNsG changes (e.g. to include a calculation model prior to rinsing studies), this change will also apply to this document.

[8] The threshold levels can be found in Appendix I, Table I.1, section 5.1 to the "Guidance on Estimating Transfer of Biocidal Active Substances into Foods – Professional Uses" (under development)

[9] Please note that this is the current proposal in the Food TNsG which has not been finalised. If the approach in the Food TNsG changes (e.g. migration studies may not be required in all cases), this change will also apply to this document.

packaging). If we assume that the concentrations of the a.s. for the different uses are approximately equal (e.g. the a.s. concentration in an ink is approximately equal to the a.s. concentration in a coating), we can assume that some uses have very limited exposure compared to other uses. As a result, these uses would not be considered worst-case uses. For example, if the a.s. concentration in an ink (used on food packaging) is approximately equal to the a.s. concentration in a coating (used on food packaging), the use in ink could be disregarded because the contact surface of the ink with food is much smaller than the contact surface of the coating with food.
The following use categories can be excluded from the list of worst-case exposure scenarios in dietary exposure scenario 6, because of limited exposure compared to the other uses:

- **Inks and Adhesives** - Inks and adhesives are used in food packaging materials, but the contact surface with the food is low when compared to the contact surface with other PT6 residues (e.g. in polymer dispersions).

- **Mineral slurries** - Mineral slurries are used in the production of food packaging. However, this results in a high dilution in the finished product. Compared to other food contact materials (e.g. those made from a preserved polymer dispersion or coated with a PT6 treated coating), the active substance concentration in the paper is assumed to be low. As stated in the TNsG on Human Exposure, "many biocides degrade in paper-making, so in-use concentrations are lower than the nominal values"[10]. INERIS further informs that "for in-can preservatives (PT6), the substance is not designed for fixation onto fibres and it can be assumed that no specific fixation occurs[11]".

- **Coatings** - Coatings are used on food packaging to protect the packaging and the food, may come in direct contact with food.

- **Polymer dispersions** – Polymer dispersions form the basis of food contact materials, and therefore come in direct contact with food.

Based on these assumptions, Coatings and Polymer dispersions can be considered the worst case for scenario 6.

These assumptions can only be made if the concentration of the a.s. in the preserved products is in the same order of magnitude. If the a.s. concentration in the use categories *Inks*, *Adhesives* or *Mineral Slurries* is much higher compared to e.g. a coating or a polymer dispersion, it cannot automatically be assumed that exposure from these categories is negligible. In this case, the amount of a.s. in the finished food contact material (e.g. the amount of a.s. from ink in relation to the packaging on which the ink is printed) should be investigated.

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[10] TNsG on Human Exposure, part 2, 2002, (pp. 98, type 12.01 slimicides for paper pulp)
[11] Institut national de l'environnement industriel et des risques (INERIS). DRC-01-255582-ECOT-CTi/VMi-nº01DR0183.doc. Supplement to the methodology for risk evaluation of biocides: Emission scenario document for biocides used in paper coating and finishing (Product type 6, 7 & 9), May 2001: http://ihcp.jrc.ec.europa.eu/our_activities/public-health/risk_assessment_of_Biocides/doc/ESD/ESD_PT/PT_06/PT_6_PT_7_PT_9_Paper_coating_and_finishing.pdf/view

Worst case for dietary exposure scenario 6: Coatings and Polymer Dispersions

Dietary exposure scenario 7:

As identified in Table 3, dietary exposure scenario 6 includes the following use category:

- Mineral Slurries

In addition to food packaging, *Mineral slurries* can also be formulated into packaging paper for animal feed. According to the Livestock TNsG, scenario 7 is assessed by calculating the exposure of the livestock animal, which results in a statement about the relevance of human dietary exposure by consuming food from the exposed animal.

PT6 residues in mineral slurries formulated into packaging paper for feed have an additional intermediate (the animal) before they reach the consumer. It can therefore be assumed that mineral slurries formulated into packaging paper for feed are covered by the assessment of packaging paper for food. In this example, mineral slurries formulated into packaging paper for food are assumed to be covered by the assessment of coatings. Therefore, mineral slurries formulated into packaging paper for feed are also covered by the assessment of coatings. Whether this assumption also applies in cases where animal-specific metabolites are formed and/or accumulation in the animal occurs, must be decided on a case-by-case basis.

Worst case for scenario 7: None, because it is covered by dietary exposure scenario 6.

Methodology for an example product: STEP C

As a final step, the dietary risk of the worst-case use in each dietary exposure scenario is assessed.

Based on the assumptions above, the following PT6-relevant uses were identified as worst-case uses in this particular example taken from the HEEG opinon:

Table 4 Worst-case use in each dietary exposure scenario

Non-professional dietary exposure scenario:	**Worst-case use**
Scenarios 1, 2 and 3 Liquid detergents, Household Cleaners/Disinfectants, Household Insecticides	the use with the highest calculated exposure value
Professional dietary exposure scenario:	**Worst-case use**
scenario 4 Industrial/Institutional Insecticides	none; not applicable
scenario 5 Industrial/Institutional Cleaners/Disinfectants	the use with the highest calculated residue per unit area before rinsing
scenarios 6 (FCM) Coatings, Inks, Polymer Preservation, Adhesives, Mineral Slurries	coatings and polymer dispersions
scenario 7 (feed packaging) Mineral slurries	none; covered by scenario 6

An aggregate exposure assessment of the identified worst-case uses should be performed. However, at the moment no harmonised criteria for a quantitative aggregate exposure assessment exist at EU-level. Therefore, until agreed criteria have been established, only a qualitative aggregate assessment should be performed.

Conclusion:

This example illustrates how to identify the worst-case use categories for a biocidal product within PT6 in order to minimise the number of use categories for which a dietary exposure and risk assessment must be performed. The worst-case use categories presented here are specific to the particular example presented here and may well differ for PT6 products with other use patterns and use combinations. Therefore, depending on the use patterns of the products in PT6, applicants need to undertake considerations on the range of their PT6 uses which might have relevance for dietary exposure. The exposure scenario building process used to arrive at the conclusion here must be undertaken for each individual PT6 biocidal product and explained in the application for product authorisation. The example in this paper can be used as a guide.