Addendum relevant to Biocides to the TGD on Risk Assessment

(Endorsed at the 23rd CA meeting Nov. 2006)

$PNEC_{oral}$ derivation for the primary and secondary poisoning assessment of anti-coagulant rodenticides

Derivation of PNECoral for primary and secondary poisoning has been discussed at the Biocides TM I '06 when discussing the substances difethialone and coumatetralyl. Norway provided a discussion document which resulted in the following guidance.

There was a general agreement that the principles laid down in the TGD do not reflect the special situation with regard to rodenticides very well. In addition to the secondary poisoning assessment from the TGD ($PEC_{oral,\ fish}$ and $PEC_{oral,\ worm}$ compared to a PNEC for fish- or worm-eating mammals or birds) another food chain rodenticide (bait) →rodent →rodent-eating mammal or rodent-eating bird has to be assessed here. A predicted environmental concentration, which corresponds to the $PEC_{oral,\ predator}$ in the TGD needs to be defined. According to the emission scenario developed for product type 14 in the EUBEES project "…it will then be compared with the predicted no-effect concentration $PNEC_{oral}$ according to the TGD". However, the guidance for PNEC derivation given in the TGD refers to an exposure situation which is completely different from the exposure situation for rodenticides. Also in the ESD PT14 it is questioned "…if the $PNEC_{oral}$ calculated according to the TGD is really very suitable for rodenticides".

One issue not yet discussed at TM regarding $PNEC_{oral}$ derivation for the primary and secondary poisoning assessment of rodenticides is whether it is considered necessary to derive separate $PNEC_{oral}$ for an acute and a chronic exposure situation to rodenticides as done by most MS.

In ESD PT14 it is stated that "…it could be argued that both an acute and a chronic risk assessment should be done for anticoagulants, because although the mode of action is generally chronic, some anticoagulants have substantial acute toxicity." ESD PT14 states also that "…the time periods implied by the exposure and effects assessments should be comparable. If possible these two should be made consistent". The ESD PT14 gives no clear guidance on whether two separate $PNEC_{oral}$ values have to be derived and on how to do this.

The $PNEC_{oral}$ derivation described in the TGD for the secondary poisoning assessment considers the oral intake of a chemical via fish or worms and a more or less continuous exposure situation and no guidance is given at all regarding primary poisoning. The TGD does not state to derive a separate short-term $PNEC_{oral}$ in addition to the long-term $PNEC_{oral}$. Therefore no guidance is available on how to derive a short-term $PNEC_{oral.}$

At TM I '06 it was not possible to find another way of deriving $PNEC_{oral}$ than the approach described in the TGD and it was agreed to follow the TGD. However, for the short-term exposure and for primary poisoning no guidance is given in the TGD.

This document is meant as a proposal for harmonising the primary and secondary poisoning assessment of anticoagulant rodenticides so that a future comparative

assessment of anticoagulant rodenticides would be possible. It was discussed and agreed upon at TM III '06.

Item 1: Do we need both a short-term and a long-term $PNEC_{oral}$?

As described in general in the TGD only one PNEC is derived for any effects assessment, which, if not exceeded, should ensure an overall protection of the environment. This PNEC can be considered as a long-term value.

The situation with respect to anticoagulant rodenticides is different. Most anticoagulant rodenticides are acutely toxic to mammals and birds and there is the possibility of an acute poisoning situation in addition to a long-term exposure of non-target mammals and birds. This situation is not reflected in the TGD, however, it is considered especially relevant for primary poisoning, whereas for secondary poisoning the long-term exposure seems to be more relevant than the acute exposure situation.

Comparing an acute poisoning incident, which represents a single uptake of the anticoagulant rodenticide by a non-target mammal or a bird, with a $PNEC_{oral}$ which has been derived in accordance with the TGD, considerably overestimates the risk due to the choice of long-term studies as a basis for deriving the $PNEC_{oral}$.

On the other hand no guidance is available on how to derive $PNEC_{oral}$ values for an acute poisoning situation. Every MS which derived short-term $PNEC_{oral}$ values for their evaluations chose its own approach. Different studies, different endpoints and different assessment factors have been used as no harmonised guidance is available at the moment. When discussing this issue it became clear that the situation is that complex that it will not be possible to reflect the real life situation in the primary and secondary poisoning assessments of the evaluation reports. It remains unclear which studies should be chosen for a derivation of an acute $PNEC_{oral}$ and also which assessment factors should be applied to them. Due to these problems it is considered more than difficult to reach a compromise regarding the derivation of a $PNEC_{oral}$ for acute poisoning situations. Having in mind the importance of harmonising the primary and secondary poisoning assessment of anticoagulant rodenticides for a future comparative assessment the following pragmatic approach is suggested for the time being. When revising the ESD PT14, guidance should be included on how to derive a $PNEC_{oral}$ for acute exposure situations.

Qualitative risk assessment for acute situation

At the moment it is suggested not to conduct a quantitative risk assessment for the acute primary as well as the acute secondary poisoning situation. Instead a qualitative description of the toxicity of the substance compared to the possible single uptake should be given.

Example primary poisoning Tier 2, single uptake without excretion:

Concentration of active substance in bait 25 mg/kg

Tree sparrow: daily food uptake 7.6 g/day

Body weight: 22 g

Expected content of the active substance in the sparrow for a single uptake incident if the sparrow consumes 100% of its daily food uptake on rodenticide bait: 8.64 mg/kg bw

LD50 of the active substance (bird) = 0.264 mg/kg bw

From this calculation it becomes clear that the sparrow dies if consuming 100% of its daily food uptake on rodenticide bait, even without applying an assessment factor to a single dose LD50. The same comparison can be made for an acute situation at Tier 1 secondary poisoning with Frodent = 1.

It is important to stress that this qualitative assessment is not intended to be used for the risk assessment of primary and secondary poisoning of rodenticides. This comparison only gives a first indication of the acute toxicity of the substance. If an anticoagulant rodenticide with a lower acute toxicity e.g. has a LD 50 (bird) which is above the expected content in the sparrow the conclusion of this comparison should NOT be that the substance is not acutely toxic or "unproblematic" with regard to the acute primary poisoning situation because a comparison is made with a single dose LD50 without applying an assessment factor. This comparison is not intended to be used for risk characterisation: no PNEC shall be derived and hence no PEC/PNEC ratio can be established, and shall not be used for a comparative assessment.

Object of a qualitative risk assessment should be:

- Primary poisoning:
    - Tier 2 for 1 days exposure with and without excretion, where the PEC_{oral} is the expected concentration of the active substance in the non-target animal after 1 day exposure (single meal) [mg/kg bw]. A default excretion factor of 0.3 (for birds and mammals) should be used in case no data is available. For a first step worst case, the parameter AV*, PT and PD are all 1. For a more realistic worst case AV* = 0.9, PT = 0.8 and PD = 1.
- Secondary poisoning
    - Tier 1, where the PEC_{oral} is the concentration in the rodent immediately after a last meal on day 5 [mg/kg food]. For a short-term exposure PD is 1 (rodents have fed entirely on rodenticide) and Frodent = 1 (non-target animals consume 100 % of their daily intake on poisoned rodents). For comparison calculations with PD = 0.5 and PD = 0.2 could also be included.

Quantitative risk assessment for long-term situation

For the long-term exposure, as described in the ESD PT14, a quantitative risk assessment for primary and secondary poisoning should be carried out. For that the $PNEC_{oral}$ should be derived in accordance with the TGD.

* AV has to be set to 0.5 for birds if the product is a paste in an envelope

Object of a quantitative risk assessment should be:

- Primary poisoning:
    - Tier 1 where the PEC_{oral} is the concentration of the activessubstance in the food (bait) [mg/kg food]
    - Tier 2 for 5 days exposure, considering excretion, where the PEC_{oral} is the expected concentration of the active substance. in the non-target animal after 5 days exposure [mg/kg bw]. A default excretion factor of 0.3 (for birds and mammals) should be used in case no data are available. As a worst case, the parameter AV*, PT and PD are all 1.
- Secondary poisoning
    - Tier 1 for a long-term exposure. The PEC_{oral} is the concentration in the rodent immediately after a last meal on day 5 [mg/kg food]; PD = 1 and Frodent = 0.5 (non-target animals consume 50 % of their daily intake on poisoned rodents). For comparison calculations with PD = 0.5 and PD = 0.2 could also be included.
    - Tier 2 for a long-term exposure. The PEC_{oral} is the concentration in non-target animals after a single day of exposure [mg/kg bw]; PD = 1 and Frodent = 0.5.

For a comparative assessment the long-term PEC/PNEC values of the respective substances should be compared. As a worst case, PEC/PNEC ratios of the smallest bird and the smallest mammal should be compared for primary as well as secondary poisoning.

Item 2: Choice of studies for the long-term risk assessment for primary and secondary poisoning

It is suggested using the NOEC from an avian reproduction study or, if not available, the LC50 from a 5 days feeding study with birds for $PNEC_{oral,\ bird}$ derivation.

For mammals the NOAEL from a 28 or a 90 days repeated dose toxicity study or from a chronic study should be used.

For converting the $PNEC_{oral}$ values from a concentration in food [mg/kg food] to a dose related $PNEC_{oral}$ [mg/kg body weight], and vice versa, the following equation should be used:

*Daily dose [mg/kg bw day] = conc. in food [mg/kg] * daily food consumption [g/bird day]/body weight [g]*

Data from animals used in the test should be used for conversion (i.e. body weight and daily food intake of the test species) and not default values given in EUBEES.

Item 3: Assessment factors

The AF laid down in the TGD should be used for $PNEC_{oral}$ derivation for the long-term risk assessment.