Based on the re-evaluation of the available data set, RMS proposes to change the reference dose derived during the initial peer-review. In the available repeat-dose toxicity studies, dogs and rabbits were usually the most sensitive species. Administration durations of these short-term studies were relevant for setting the AOEL. The outlying NOAELs in one 90-day rat study with metolachlor and the offspring effects in the multigeneration study with metolachlor are considered more related to dose selection than indicative of higher toxicity. When comparing the NOAELs seen in the short-term studies in dogs (10 or 15 mg/kg bw/d for 1-yr or 90-d studies, respectively) and in the dermal short-term study in rabbits (10 mg/kg kg bw/d), it is considered better to select the lower value. Hence, RMS proposes:

AOEL: 0.1 mg/kg bw per day
based on 1-year study in dogs, SF 100
correction for limited oral bioavailability is not necessary.

The applicants supported the previous reference dose of 0.15 mg/kg bw per day.

The Co-RMS indicated the the AOEL should be derived based on the NOAEL for offspring effects in the multigeneration study with metolachlor of 2.4 mg/kg bw/d, an AF of 100 and no correction for limited bioavailability, leading to 0.024 mg/kg bw per day. The different NOAELs could reflect higher sensitivity of developing organisms. The LOAEL for offspring toxicity in the multi-generation study was 24 mg/kg bw/d.
Furthermore CoRMS proposed a NOAEL of 3.5/3.6 mg/kg bw/d (males/females) for the 1-year dog study and regarded 9.7 mg/kg bw/d as LOAEL based on decreased bodyweight gain in females.
The different positions of RMS and CoRMS regarding the point of departure to establish the reference dose are an issue of disagreement and an issue for expert consultation.

With respect to the derivation of an AAOEL it is noted that currently no harmonized guidance document is available for setting an AAOEL. Thus, no proposal for an AAOEL is given. However, if it is justified to set an AAOEL, the same point of departure as for the ARfD should be used (0.5 mg/kg bw per day, based on developmental toxicity study in rats, SF 100, correction for limited oral bioavailability is not necessary).
The applicants did not assess the need for an AAOEL.

2.6.14 Summary of product exposure and risk assessment

A9396G containing 960 g/L S-metolachlor is used as a pre- or post-emergence herbicide on maize and sunflower at a maximum application rate of 1.5 L product per hectare. Dermal absorption data for S-metolachlor in A9396G were obtained from an in vitro study on human skin. For the concentrate a value of 0.4% and for the highest tested dilution (2.4 g/L) a value of 13% were derived. Operator exposure estimated according to EFSA guidance was above the AOEL without PPE (34% with work wear). Worker exposure during re-entry activities is acceptable when work wear is worn (26% of the AOEL). Bystander exposure and resident exposure is below the AOEL (max. 43% of the AOEL). However, further evaluation of the risk for bystanders with respect to the sensitising potential of the spray solution is needed.

2.7 Residues

2.7.1 Summary of storage stability of residues

The storage stability of S-metolachlor in frozen crop matrices was evaluated during the initial EU Review of the active substance by the RMS Belgium in August, 2000 (ASB2010-10547). The submitted studies were considered to be acceptable by the RMS. However, due to analysis of metolachlor hydrolysates only, the deficiencies of the analytical methods and the fact that residue values were mostly