TOXICITY TESTING METHODS TO BE USED BY THE REACH REGULATION

COUNCIL REGULATION (EC) No 440/2008 of 30 May 2008 laying down test methods pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)

(1) Pursuant to Regulation (EC) No 1907/2006, test methods are to be adopted at Community level for the purposes of tests on substances where such tests are required to generate information on intrinsic properties of substances.
(2) Council Directive 67/548/EEC of 27 June 1967 on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances laid down, in Annex V, methods for the determination of the physico-chemical properties, toxicity and ecotoxicity of substances and preparations. Annex V to Directive 67/548/EEC has been deleted by Directive 2006/121/EC of the European Parliament and of the Council with effect from 1 June 2008.
(3) The test methods contained in Annex V to Directive 67/ 548/EEC should be incorporated into this Regulation.
(4) This Regulation does not exclude the use of other test methods, provided that their use is in accordance with Article 13(3) of Regulation 1907/2006.
(5) The principles of replacement, reduction and refinement of the use of animals in procedures should be fully taken into account in the design of the test methods, in particular when appropriate validated methods become available to replace, reduce or refine animal testing.
(6) The provisions of this Regulation are in accordance with the opinion of the Committee established under Article 133 of Regulation (EC) No 1907/2006

Article 1: The test methods to be applied for the purposes of Regulation 1907/2006/EC are set out in the Annex to this Regulation.
Article 2: The Commission shall review, where appropriate, the test methods contained in this Regulation with a view to replacing, reducing or refining testing on vertebrate animals.
Article 3: All references to Annex V to Directive 67/548/EEC shall be construed as references to this Regulation.
Article 4: This Regulation shall enter into force on the day following its publication in the *Official Journal of the European Union*.
It shall apply from 1 June 2008.

LIST OF METHODS FOR THE DETERMINATION OF TOXICITY

B.1 bis. Acute oral toxicity – fixed dose procedure
B.1 tris. Acute oral toxicity – acute toxic class method
B.2. Acute toxicity (inhalation)
B.3. Acute toxicity (dermal)
B.4. Acute toxicity: dermal irritation/corrosion
B.5. Acute toxicity: eye irritation/corrosion
B.6. Skin sensitisation
B.7. Repeated dose (28 days) toxicity (oral)
B.8. Repeated dose (28 days) toxicity (inhalation)
B.9. Repeated dose (28 days) toxicity (dermal)
B.10. Mutagenicity – *in vitro* mammalian chromosome aberration test
B.11. Mutagenicity – *in vivo* mammalian bone marrow chromosome aberration test
B.12. Mutagenicity – *in vivo* mammalian erythrocyte micronucleus test
B.13/14. Mutagenicity: reverse mutation test using bacteria
B.15. Mutagenicity testing and screening for carcinogenicity gene mutation – *saccharomyces cerevisiae*
B.16. Mitotic recombination – saccharomyces cerevisiae
B.17. Mutagenicity – in vitro mammalian cell gene mutation test
B.18. Dna damage and repair – unscheduled dna synthesis – mammalian cells *in vitro*
B.19. Sister chromatid exchange assay *in vitro*
B.20. Sex-linked recessive lethal test in *drosophila melanogaster*
B.21. *In vitro* mammalian cell transformation tests
B.22. Rodent dominant lethal test
B.23. Mammalian spermatogonial chromosome aberration test
B.24. Mouse spot test
B.25. Mouse heritable translocation
B.26. Sub-chronic oral toxicity test repeated dose 90-day oral toxicity study in rodents
B.27. Sub-chronic oral toxicity test repeated dose 90-day oral toxicity study in nonrodents
B.28. Sub-chronic dermal toxicity study 90-day repeated dermal dose study using
Rodent species
B.29. Sub-chronic inhalation toxicity study 90-day repeated inhalation dose studusing rodent species
B.30. Chronic toxicity test

B.31. Prenatal developmental toxicity study
B.32. Carcinogenicity test
B.33. Combined chronic toxicity/carcinogenicity test
B.34. One-generation reproduction toxicity test
B.35. Two-generation reproduction toxicity study
B.36. Toxicokinetics
B.37. Delayed neurotoxicity of organophosphorus substances following acute exposure
B.38. Delayed neurotoxicity of organophosphorus substances 28 day repeated dose study
B.39. Unscheduled dna synthesis (uds) test with mammalian liver cells *in vivo*
B.40. *In vitro* skin corrosion: transcutaneous electrical resistance test (ter)
B.40 bis. *In vitro* skin corrosion: human skin model test
B.41. *In vitro* 3T3 NRU phototoxicity test
B.42. Skin sensitisation: local lymph node assay
B.43. Neurotoxicity study in rodents
B.44. Skin absorption: *in vivo* method
B.45. Skin absorption: *in vitro* method