ANNEX VIII

ADDITIONAL INFORMATION AND TESTS REQUIRED UNDER ARTICLE 7 (2)

If it is not technically possible or if it does not appear scientifically necessary to give information, the reasons shall be clearly stated and be subject to acceptance by the competent authority.

The name of the body or bodies responsible for carrying out the studies shall be indicated.

LEVEL 1

Where, in accordance with the provisions of Annex VII.A related to intermediates, the relevant competent authority has authorised the application of a reduced test package to a chemical substance, the requirements of this section shall be reduced as follows.

When the quantity of the substance placed on the market reaches 10 tonnes per year per manufacturer or when the total quantity of the substance placed on the market reaches 50 tonnes per manufacturer; in this case the relevant competent authority shall require all those test and studies laid down in points 3 to 6 of Annex VII.A (excepting those already performed); in addition, the relevant competent authority may require those Level 1 tests and studies related to aquatic organisms.

When the quantity of the substance placed on the market reaches 100 tonnes per year per manufacturer or when the total quantity of the substance placed on the market reaches 500 tonnes per manufacturer; in this case the relevant competent authority shall require the Level 1 tests or studies related to reproductive toxicity. The relevant competent authority may decide that the classification of the substance as an intermediate qualifying for a reduced test package constitutes a good reason why one or more tests and studies, except those related to reproductive toxicity, are not appropriate.

Physico-chemical studies

Further studies on physico-chemical properties dependent upon the results of the studies laid down in Annex VII. Such further studies could include for example the development of analytical methods which make it possible to observe and detect a substance or its transformation products and studies on thermal decomposition products.

Toxicological studies

Fertility study (one species, one generation, male and female, most appropriate route of administration).

If there are equivocal findings in the first generation, study of a second generation is required.

Depending upon the dosing schedule it may be possible in this study to obtain an indication of teratogenicity. A positive indication should be examined in a formal teratology study.

- Teratology study (one species, most appropriate route of administration)

This study is required if teratogenicity has not been examined in the fertility study.

- Sub-chronic and/or chronic toxicity study, including special studies (one species, male and female, most appropriate route of administration) shall be required if the results of the repeated-dose study in Annex VII or other relevant information demonstrate the need for further appropriate investigation.

The effects which would indicate the need for such a study could include for example:

(a) serious or irreversible lesions;

(b) a very low or absence of a "no effect" level;

(c) a clear relationship in chemical structure between the substance being studied and other substances which have been proved dangerous.

- Additional mutagenesis studies and/or screening study(ies) for carcinogenesis as prescribed in the testing strategy described in Annex V.

When both tests in the base set are negative, further tests shall be conducted according to the specific properties and the purposed use of the substance.
When a test or both tests were positive in the base set, a supplementary study should include the same or different end points in other in vivo test methods.
- Basic toxicokinetic information.

Ecotoxicity studies
- Prolonged toxicity study with Daphnia magna (21 days)
- Test on higher plants
- Test on earthworms
- Further toxicity studies with fish
- Tests for species accumulation; one species, preferably fish
- Supplementary degradation study(ies), if sufficient degradation has not been proved by the studies laid down in Annex VII
- Further studies on absorption/desorption dependent upon the results of the investigations laid down in Annex VII.

LEVEL 2

When the quantity of the substance placed on the market reaches 1,000 tonnes per year per manufacturer or when the total quantity of the substance placed on the market reaches 5,000 tonnes per manufacturer; additional studies mentioned in Level 1 or 2 would normally not be required. The relevant competent authority should however, consider additional tests and may require additional tests including the tests laid down in Levels 1 and 2 of this Annex.

Toxicological studies

The test programme shall cover the following aspects unless there are strong reasons to the contrary, supported by evidence, that it should not be followed:
- Chronic toxicity study
- Carcinogenicity study
- Fertility study (e.g. three-generation study); only if an effect on fertility has been established at level 1
- Developmental toxicity study on peri- and postnatal effects
- Teratology study (species not employed in the respective level 1)
- Additional toxicokinetic studies which cover biotransformation, pharmacokinetics
- Additional tests to investigate organ or system toxicity.

Ecotoxicological studies
- Additional tests for accumulation, degradation, mobility and absorption/desorption
- Further toxicity studies with fish
- Toxicity studies with birds
- Additional toxicity studies with other organisms.