Integrated testing strategy for mutagenicity under REACH

The substance[1] is manufactured or imported in quantities ≥ 1 tonne per year

Perform[2] *in vitro* gene mutation study in bacteria.

There is a positive result in the *in vitro* gene mutation study in bacteria.

- Yes → Consider[2] further mutagenicity studies.
- No

The substance is manufactured or imported in quantities ≥ 10 tonnes per year

- No → No further testing required.
- Yes

Adequate data from an *in vivo* cytogenicity test are available;
OR
the substance is known to be carcinogenic category 1 or 2 or mutagenic category 1, 2 or 3.

- No → Perform[2] an *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study.
- Yes

Adequate data from a reliable *in vivo* mammalian gene mutation test are available;
OR
there is a positive result in the *in vitro* gene mutation study in bacteria;
OR
there is a positive result in the *in vitro* cytogenicity study in mammalian cells or the *in vitro* micronucleus study (see above).

- No → Perform[2] an *in vitro* gene mutation study in mammalian cells.
- Yes

There is a positive result in any of the genotoxicity studies previously considered.

- Yes → Consider[2] further *in vivo* mutagenicity studies.
- No

The substance is manufactured or imported in quantities ≥ 100 tonnes per year

- No → No further testing required.
- Yes

There is a positive result from an *in vivo* somatic cell study available.

- Yes → Consider the potential for germ cell mutagenicity on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, consider[2, 3] additional investigations.
- No

There is a positive result in any of the *in vitro* genotoxicity studies previously considered;
AND
There are no results available from an *in vivo* study already.

- Yes → Propose[2, 3] an appropriate *in vivo* somatic cell genotoxicity study.
- No

The substance is manufactured or imported in quantities ≥ 1000 tonnes per year

- No → No further testing required.
- Yes

There is a positive result in any of the *in vitro* genotoxicity studies previously considered.

- Yes → Propose[2, 3] a second *in vivo* somatic cell genotoxicity test, depending on the quality and relevance of all the available data.
- No

There is a positive result from an *in vivo* somatic cell study available.

- Yes → Consider the potential for germ cell mutagenicity on the basis of all available data, including toxicokinetic evidence. If no clear conclusions about germ cell mutagenicity can be made, consider[2, 3] additional investigations.
- No

No further testing required.

1. The substances concerned are:
(a) non-phase-in substances manufactured or imported in quantities of 1 to 10 tonnes;
(b) phase-in substances manufactured or imported in quantities of 1 to 10 tonnes and meeting the criteria in annexe III;
(c) phase-in substances not meeting the criteria in annexe III and manufactured or imported in quantities of 10 tonnes or more.

2. A registrant may adapt the standard testing regime in accordance with the general rules set out in annexe XI section 1 (Testing does not appear scientifically necessary) and 2 (Testing is technically not possible). Under dossier evaluation the Agency may assess these adaptations to the standard testing regime.

3. Testing may be omitted, based on the exposure scenario(s) developed in the Chemical Safety Report as mentioned in annexe XI, section 3 (Substance-tailored exposure-driven testing).

cnrs

Prévention du risque chimique, France, 2007

REACH Registration, Evaluation, Authorisation of Chemicals