Integrated testing strategy for mutagenicity under REACH

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

Perform in vitro gene mutation study in bacteria.

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

Yes

Consider further mutagenicity studies.

No

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

Yes

Perform in vitro cytogenicity study in mammalian cells or an in vitro micronucleus study.

Adequate data from an in vivo cytogenicity test are available;

Yes

No further testing required.

OR

the substance is known to be carcinogenic category 1 or 2 or mutagenic category 1, 2 or 3.

No

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

Yes

Adequate data from a reliable in vivo mammalian gene mutation test are available;

Yes

Consider further mutagenicity studies.

No

Perform an in vitro gene mutation study in mammalian cells.

OR

the substance is known to be carcinogenic category 1 or 2 or mutagenic category 1, 2 or 3.

No

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

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 additional investigations.

No

Propose an appropriate in vivo somatic cell genotoxicity study.

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

Yes

Propose 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 study already.

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

Yes

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

No

There are no results available from an in vivo study already.

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 additional investigations.

No

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

There is a positive result from an in vivo study already.

Yes

No further testing required.

No

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

Yes

No further testing required.

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

Yes

Propose a second in vivo somatic cell genotoxicity test, depending on the quality and relevance of all the available data.