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GENETIC TOXICOLOGY

FOR PHARMACEUTICALS, MEDICAL DEVICES, COSMETICS, INDUSTRIAL CHEMICALS: CHOOSING THE RIGHT TESTING STRATEGY

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3 MAIN AREAS IN GENOTOXICITY TESTING:

Gene Mutations	• AMES (OECD 471) • Mouse Lymphoma Assay (OECD 490) • HPRT Test (OECD 476)
Chromosome Aberration or Breakage (Clastogenicity)	• Chromosome Aberration Test (OECD 473, 475)
Chromosome Loss or Gain (Aneuploidy)	• Micronucleus Assay (OECD 478, 474)

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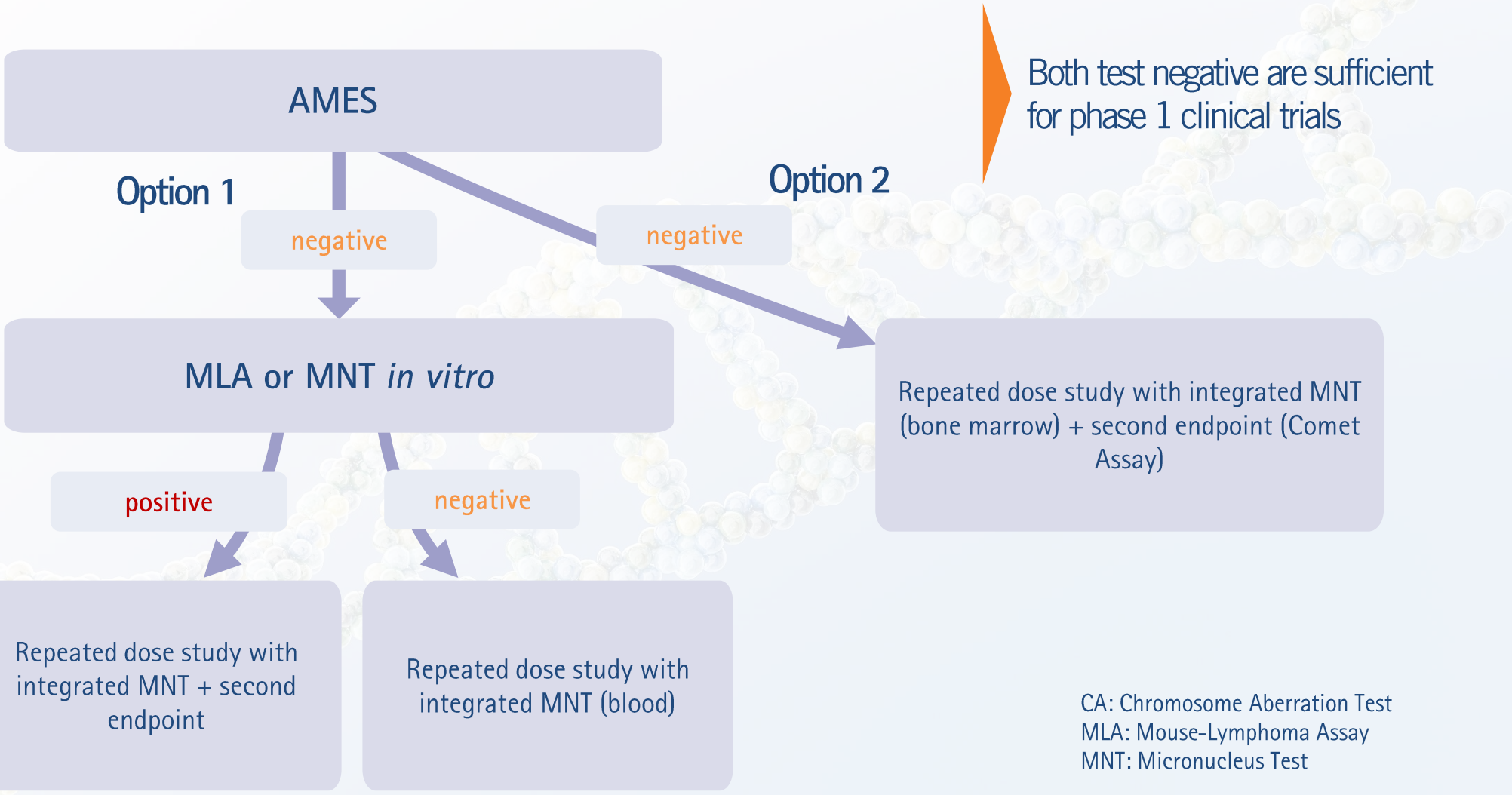
POSSIBLE FOLLOW-UP EVALUATIONS (IN CASE OF POSITIVE RESULTS):

- *in vivo* Micronucleus Test (OECD 474)
- *in vivo* Chromosome Aberration Test (OECD 475)
- *in vivo* Comet Assay (OECD 489)
- Combination of Micronucleus Test with Comet Assay (OECD 474 + 489)
- Comet with 3D-reconstructed human Skin Model
- Micronucleus Test with 3D-reconstructed human Skin Model

*All *in vivo* assays are performed by our partner lab

PHARMACEUTICALS: TESTING STRATEGY



CA: Chromosome Aberration Test
MLA: Mouse-Lymphoma Assay
MNT: Micronucleus Test

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DECISION TREE FOR IMPURITY ASSESMENT IN PHARMACEUTICALS

Starting material, Intermediates, reagents

Identification of impurity

Class 1 or 2

Control not more than TTC or others

Class 4 or 5

No further action. In case of the impurity greater than 1 mg/day, ICH Q3A/B could be considered

Class 3

Conduct GTI assesment: Is the impurity greater TTC level?

No

Yes

Reduce to not more than TTC or clarify ist mutagenicity by *in vivo* gene mutation study

No srtructual alert

(Q)SAR?

Structural alert

Ames test

Ames positive

Ames negative

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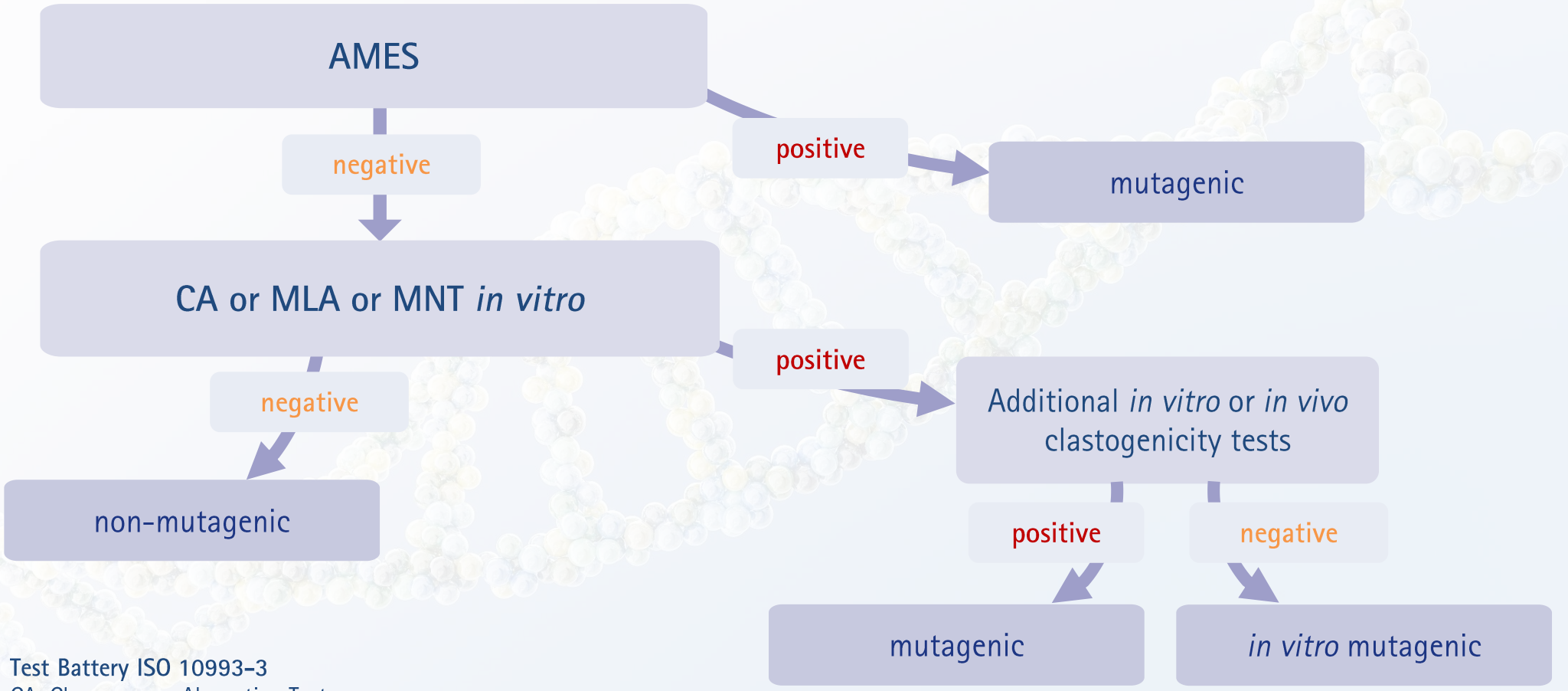
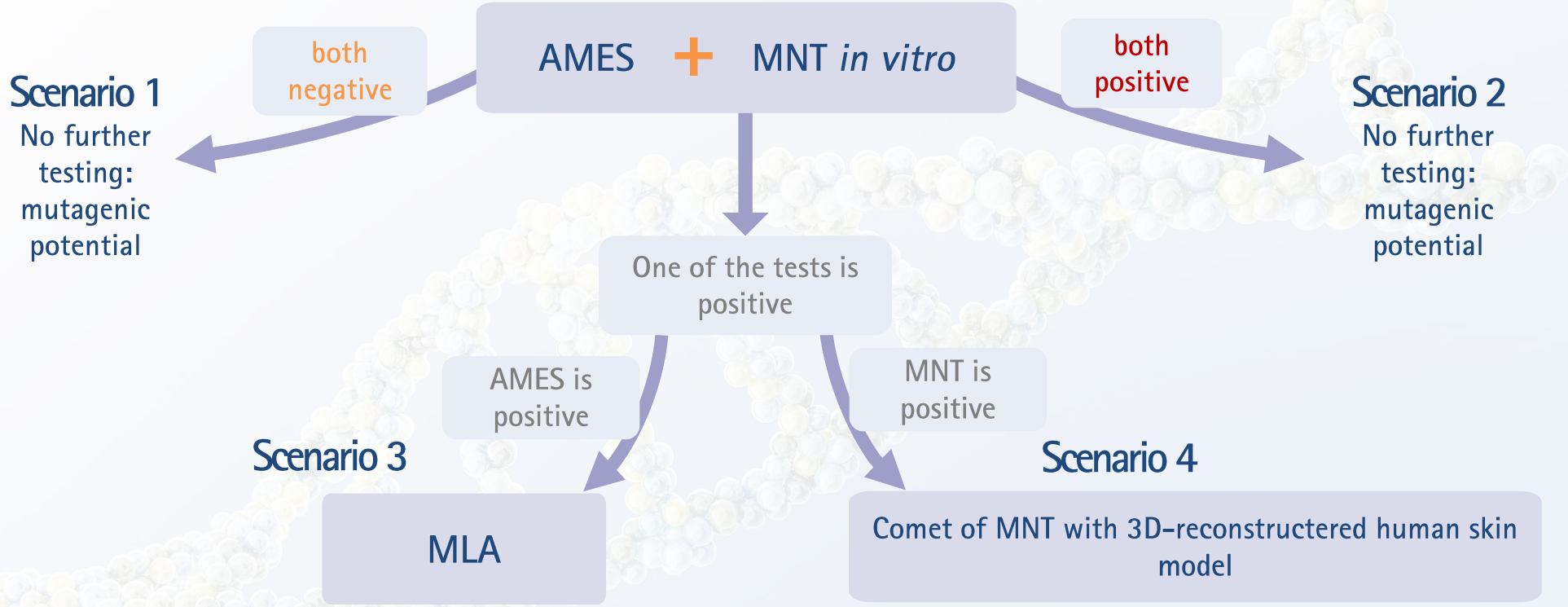
MEDICAL DEVICES: TESTING STRATEGY



Test Battery ISO 10993-3
CA: Chromosome Aberration Test
MLA: Mouse-Lymphoma Assay
MNT: Micronucleus Test

COSMETICS: TESTING STRATEGY



In any case, a weight of evidence approach has to be considered if the previous strategy does not lead to a clear answer. A positive *in vitro* result in genotoxicity testing is indicative for the carcinogenic potential of substances.

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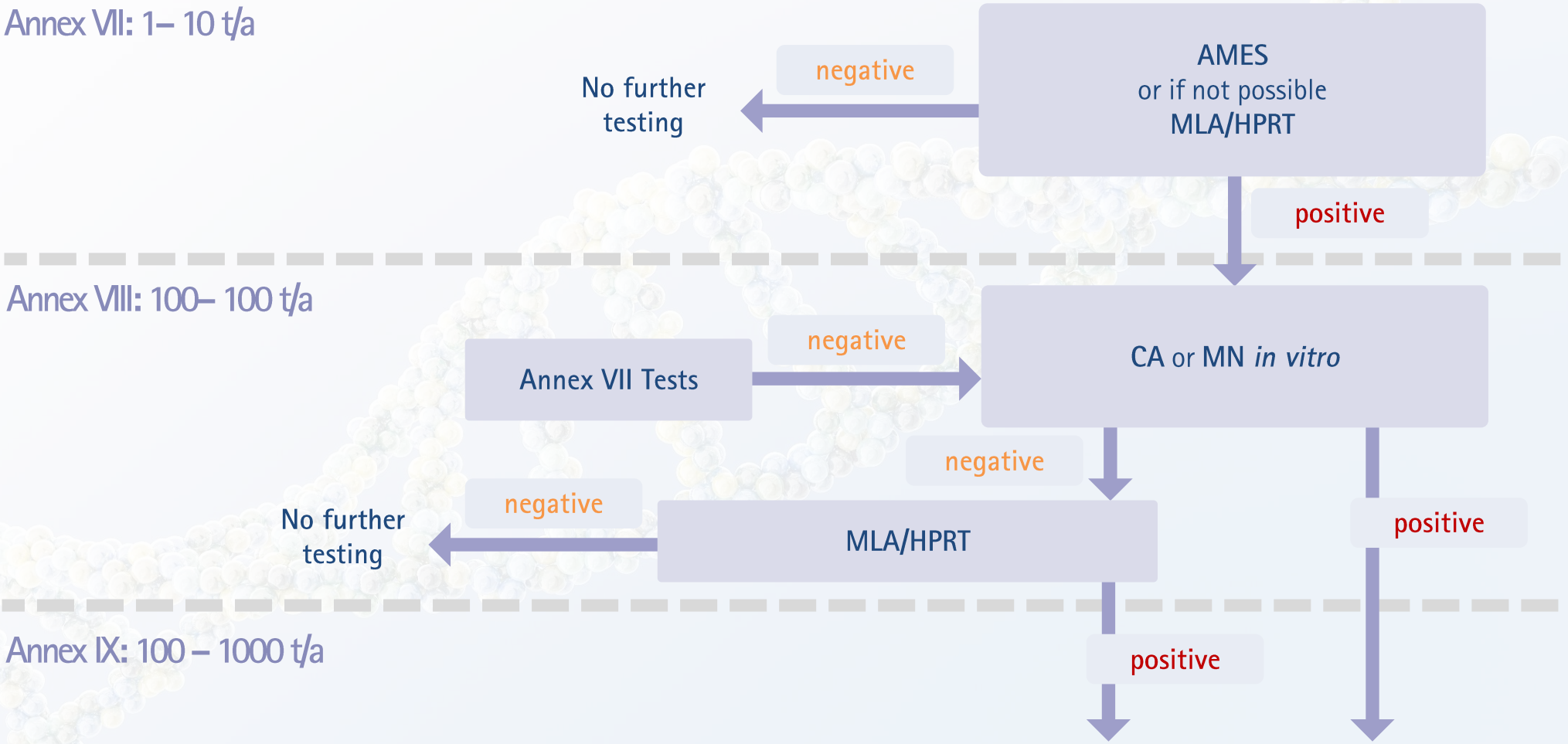
INDUSTRIAL CHEMICALS: TESTING STRATEGY



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OUR TESTING OFFER: GENETIC TOXICOLOGY SERVICES

Chromosome Damage

in vitro

- Micronucleus Assay – OECD 487
  - Chinese Hamster Cells
- Human Lymphocytes
- Chromosome Aberration Test – OECD 473
  - Chinese Hamster Cells
  - Human Lymphocytes
- 3D Skin Model combined with Micronucleus Assay - *EpiDerm® Model*

*in vivo**

- Micronucleus Assay (rat or mouse) – OECD 474
  - Peripheral Blood
  - Bone Marrow
- Chromosome Aberration Test – OECD 475
  - Bone Marrow

Gene Mutation

- Ames Test – OECD 471
- Mouse Lymphoma Assay – OECD 490
- HPRT Test – OECD 476
- Pig-a Assay

DNA Strand Breaking Properties

- Comet Assay - OECD 486
  - *in vitro*: (e.g. Chinese Hamster Cells): sponsor specific assay establishment
  - *in vivo**: Stomach, Gut, Liver, Spleen, Kidney: sponsor specific assay establishment
- Combination of Micronucleus Assay and Comet Assay
- 3D Skin Model combined with Comet Assay - *Phenion® model*

Additional Tests

- Embryonic Stem Cell Test
- Drug Uptake *in vitro*
- Hepatocyte Proliferation Assay *in vitro*
  - mouse, rat, human

*All *in vivo* assays are performed by our partner lab

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WHY CHOOSE EUROFINS?

- ✓ Our familiarity with an array of different in vitro test systems enables us to provide contract testing services using the optimum assays to answer specific product safety and efficacy questions.
- ✓ In addition to standard testing, we offer consultation concerning your specific project with regard to scientific and regulatory requirements.
- ✓ We will provide you with the most reliable and timely results possible.
- ✓ We offer several standard tests as top priority with outstanding short turnaround time.

With more than **30 years of experience** in performing biological safety and activity testing, Eurofins BioPharma Product Testing offers confirmed expertise in a broad range of Genetic & Alternative Toxicology Studies. Our tests comply with the current international guidelines (e.g. **ICH, US-FDA, ISO, EMEA, OECD**) and are performed in accordance with **GLP (Good Laboratory Practice)** to ensure their acceptability worldwide.

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