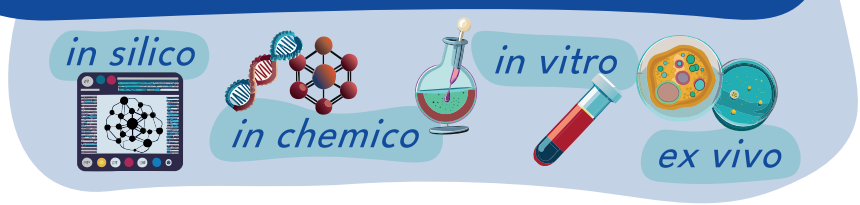
VALIDATION AND REGULATORY ACCEPTANCE

of New Approach Methodologies (NAMs)

NAMs are **new approaches** can contribute to the assessment of health and environmental hazards **without the use of animals**, as well as for preclinical studies.



Development

To ensure the development of a NAM in compliance with **international quality standards**, it is important to refer to existing guides, such as the OECD[1] Guidance Document on **Good In Vitro Method Practices** (GIVIMP) and **Guidance Document 34** (GD34[2]) on the validation of test methods.

To be used for regulatory

Validation

of a method means estabing its **reliability** (reproducibility and repeatability) and its **relevance** (predictive and regulatory). This validation study can be organised by the developing laboratory or with the help of a **validation body** (such as ECVAM[3]). In both cases, multi-laboratory **round-robin tests** are to be expected.

By adhering to documents such as:

- GD34[2]
- Good Laboratory Practices[4]

L'EURL ECVAM[3] is a major actor in validation processes at European level. It operates in consultation with its own **consultancy bodies** and its various **networks:**

- ESAC[5] assesses the scientific quality of studies
- PARERE[6] gives a preliminary opinion on the regulatory relevance of the submitted methods
- NETVAL[7] can be used to carry out the round-robins

When confidence in the NAM is established

Regulatory acceptance

of a method involves its **adoption** and **implementation** in various decision-making contexts.

This can be:

- Acceptance of the method on a «case-by-case» basis

  In the pharmaceutical sector, for example, a NAM used to test a drug is examined when the marketing authorization dossier is reviewed for approval.

- The standardisation of a NAM, through its integration into a **guideline**

  Through, for example : OECD[1]

  The guidelines provide a **framework** for conducting the tests (presentation of data, interpretation, etc.).

OECD[1]

The **proposed guidelines** are submitted to the OECD through the national coordinators. The relevance of the proposal is discussed before the **adoption** of the guideline and the rounds of public comments.

Mutual Acceptance of Data (MAD) requires a country to accept a study carried out in another OECD member country.

- avoids duplication of tests
- promotes cooperation between authorities

Validation and **standardisation** of NAMs by the OECD facilitate the **acceptance of data** from NAMs by the regulators from evaluation authorities such as ECHA[8], EFSA[9], and EMA[10].

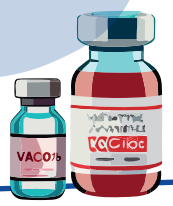
What about the pharmaceutical industry?

NAMs can be used for preclinical and clinical studies in drug development, but also for their quality control.

VACCINES and quality control

Physico-chemical methods are used to control the quality of synthetic drugs, but they may not be adapted to vaccines, which can contain biological materials that are too complex for assessment by these methods.

Thus, NAMs are increasingly used, standardised, and recognised for controlling the quality of vaccines.



The **major actors** in the implementation of NAMs in pharmaceuticals are :

- European Pharmacopeia
- EMA
- ICH[11], VICH[12]
- WHO[13], WHOA[14]

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1 - Organisation for Economic Co-operation and Development (OCDE); 2 - The guidance document on the validation and international acceptance of new or updated test methods for hazard assessment (GD34); 3 - European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM); 4 - The Principles of Good Laboratory Practice are described in Directives 2004/9/EC and 2004/10/EC; 5 - EURL ECVAM Scientific Advisory Committee (ESAC); 6 - EURL ECVAM Network for Preliminary Assessment of Regulatory Relevance (PARERE); 7 - European Union Network of Laboratories for the Validation of Alternative Methods (EU-NETVAL); 8 - European Chemicals Agency (ECHA); 9 - European Food Safety Authority (EFSA); 10 - European Medicine Agency (EMA); 11 - International Conference on Harmonisation (ICH); 12 - International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH); 13 - World Health Organisation (WHO); 14 - World Organisation for Animal Health (WOAH).