Non-animal methods and new approach methodologies in UK REACH registration

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What do we mean by NAMS?

NAMS = non-animal methods

NAMS = new approach methodologies

Aims of UK REACH

The aims of UK REACH include:

- To provide a high level of protection of human health and the environment from the use of chemicals.
- To make the people who place chemicals on the market (manufacturers and importers) responsible for understanding and managing the risks associated with their use.
- To promote the use of alternative methods for the assessment of the hazardous properties of substances eg quantitative structure-activity relationships (QSAR) and read across.

Registration: animal testing as a last resort

Legal mandate

TITLE II

REGISTRATION OF SUBSTANCES

CHAPTER 1

General obligation to register and information requirements

Article 13

General requirements for generation of information on intrinsic properties of substances

1. Information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set out in Annex XI are met. In particular for human toxicity, **information shall be generated whenever possible by means other than vertebrate animal tests**...

2. These **methods shall be regularly reviewed and improved** with a view to reducing testing on vertebrate animals and the number of animals involved…

TITLE III

DATA SHARING AND AVOIDANCE OF UNNECESSARY TESTING

CHAPTER 1

Objectives and general rules

Article 25

Objectives and general rules

1. In order to avoid animal testing, testing on vertebrate animals for the purposes of this Regulation shall be undertaken **only as a last resort**. It is also necessary to take measures limiting duplication of other tests.

Tiered information requirements: Annexes 7 to 10

Annex 7

≥ 1 tpy

Skin / eye irritation / corrosion: *in vitro*

Skin sensitisation (*in vitro / in chemico*) (*in vivo* – LLNA)

Mutagenicity: *in vitro* study in bacteria

Acute toxicity: oral route (inhalation for nanoforms)

Annex 8

≥ 10 tpy

Skin / eye irritation / corrosion: consider *in vivo* if required

Mutagenicity: *in vitro* in mammalian cells, consider *in vivo* if event of positive results in *in vitro* studies

Acute toxicity: at least one other route

Repeated-dose toxicity: 28-day study

Reproductive toxicity: screening study

Annex 9

≥ 100 tpy

Repeated-dose toxicity: 90-day study

Reproductive toxicity: developmental toxicity study (one species); extended one-generation reproduction study (triggered)

Annex 10

≥ 1000 tpy

Genotoxicity: 2nd *in vivo* somatic cell study, germ cell study as required

Repeated-dose toxicity: additional studies may be proposed

Reproductive toxicity: developmental toxicity study (2nd species), extended one-generation reproduction study ((if not already available)

Carcinogenicity: triggered

It is the **registrant's** responsibility to determine how to meet these general requirements

What is registration information used for?

Registrants

- Classify and label substances (and mixtures)
- Chemical safety assessment (hazard, exposure, risk characterisation) (≥ 10 tpy)
- Prepare chemical safety report with exposure scenarios (≥ 10 tpy)
- Communicate information through the supply chain: safety data sheets, exposure scenarios
- Keep the information up to date

Authorities

- Identify and clarify concerns (hazards, exposure, tonnage)
- Undertake regulatory management options analysis (RMOA)
- Propose mandatory classification and labelling
- Identify substances of very high concern (SVHC) to be added to the candidate list (hazard-based)
- Recommend SVHCs for addition to the authorisation list (Annex 14)
- Propose restrictions to address unacceptable risks

Legal instruments to avoid unnecessary testing

Data sharing and joint submission

- Article 26 inquiry precedes submission of registration dossier = data sharing
- ‘One substance, one registration’

Testing proposals and third-party consultations

- Annex 9 (registrations ≥ 100 tonnes) or Annex 10 (registrations ≥ 1000 tonnes)

Rules for adaptation of standard information requirements

- General (Annex 11)
- Specific, for example:
  - At Annex 8, 28-day study not required if 90-day study is available
  - At Annex 8, reproduction screening studies not required if developmental toxicity or reproduction studies are available
  - Reproduction studies not required if the substance is known to meet the criteria for classification for development toxicity (1A or 1B; consider testing for fertility effects) or adverse effects on fertility (1A or 1B; consider testing for developmental toxicity)

General adaptations of the REACH information requirements: Annex 11

1. TESTING DOES NOT APPEAR SCIENTIFICALLY NECESSARY

    i. Use of existing data
    ii. Weight of evidence
    iii. (Q)SAR
    iv. *In vitro* methods
    v. Grouping of substances and read-across approach

    Article 13: information shall be generated in accordance with internationally-recognised test methods; and in compliance with GLP

Equivalent to data generated in accordance with Article 13 if:	
Adequate for classification & labelling and risk assessment	*Adequate coverage of key parameters / comparable exposure duration / within applicability domain*
Adequate and reliable documentation	*Scientific validity has been established*

2. TESTING IS TECHNICALLY NOT FEASIBLE
3. SUBSTANCE-TAILORED EXPOSURE-DRIVEN TESTING

UK REACH registration options

UK REACH: transitional registration arrangements

UK REACH provides different options to support the transition for new and existing registrants

Registration approach	Full information requirements*	Number received in 2021
Grandfathered (GB-based EU REACH registrants)	Oct 2023-Oct 2027	> 9000
Downstream user import notification (DUIN)	Oct 2023-Oct 2027	> 5400
New registration of an existing substance (NRES)	Oct 2023-Oct 2027	> 400
Novel substance (not registered under EU REACH prior to 1 January 2021)	At registration	< 30

Substance groups to support joint submission = ‘one substance, one registration’

* Current deadlines

Announcement on transitional registration provisions

https://www.gov.uk/government/news/deadline-for-uk-reach-to-be-extended

GOV.UK | Topics | Government activity

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News story

Deadline for UK REACH to be extended

Government to consult on UK REACH deadlines

From: Department for Environment, Food & Rural Affairs, Health and Safety Executive, and The Rt Hon George Eustice MP

Published 6 December 2021

Defra has committed to exploring alternative arrangements for UK REACH transitional registrations today in order to support chemical businesses whilst upholding the highest standards to safeguard public health and the environment.

Summary

UK REACH registration: summary

Registration information requirements

- Tiered depending upon tonnage
- The standard information requirements can be adapted in many ways
- Information should be adequate for classification & labelling and risk assessment

‘Existing’ substances

- Most registrations are for ‘existing’ substances: existing data and data sharing
- Requirements for transitional registrations are under review

‘Novel’ substances

- Most initially registered in 1-10 (lowest) tonnage band

Responsibilities of registrants

- For any adaptation: the **responsibility is on the registrant** to justify their use & demonstrate how they provide the same level of information as the standard requirement

Questions and challenges

Challenges and questions

Methods must enable hazard classification & labelling and support hazard-based regulatory actions

Accessibility of the more complex NAMs to all registrants (e.g., SMEs)

Communication and explanation of sometimes complex approaches

Acceptance by stakeholders?

- If findings from non-standard approaches result in regulatory action
- Potentially lower points of departure
- Confidence (of regulators) in ‘negative’ results
- Perceived rigour of alternative approaches compared with standard animal tests

International acceptance and familiarisation (e.g., case studies)