Some examples of KaRLs

KaRL5, KaRL6 and KaRL9

KaRL Assignment

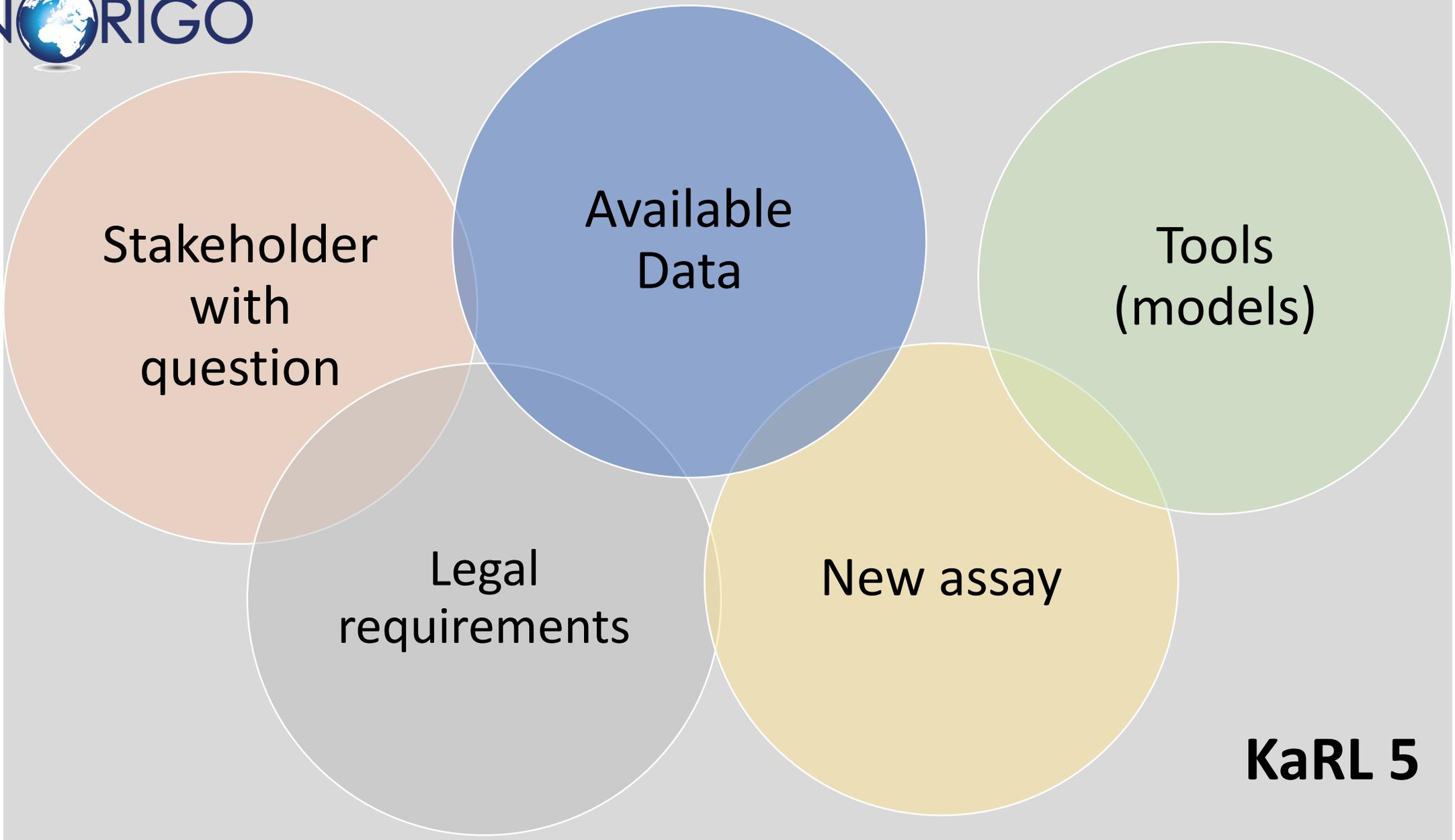| Requirements	KaRL 1	KaRL 2	KaRL 3	KaRL 4	KaRL 5	KaRL 6	KaRL 7	KaRL 8	KaRL 9
Data exist	✓	✓	✓	✓	✓	✓	✓	✓	✓
Accessibility		✓	✓	✓	✓	✓	✓	✓	✓
Metadata completeness (MINChar, MIAMETox)		✓	✓	✓	✓	✓	✓	✓	✓
Semantic metadata with toxicological context (NanoTox met.checkl.)			✓	✓	✓	✓	✓	✓	✓
OECD guidelines				✓	✓	✓	✓	✓	✓
SOPs				✓	✓	✓	✓	✓	✓
Fitness-for-Purpose criteria (Klimish, DaNa, NanoCred, GuideNano)				✓	✓	✓	✓	✓	✓
Legal requirements					✓	✓	✓	✓	✓
Can question be answered					✓	✓	✓	✓	✓
Is it an actionable document					✓	✓	✓	✓	✓
Is an actionable document quality checked: fullfills requirements						✓	✓	✓	✓
Actionable document is traceable							✓	✓	✓
Requiremets for broad context								✓	✓
SEIN								✓	✓
Circular Economy								✓	✓
Safer-by-Design								✓	✓
Good governance principles								✓	✓
Does an actionable document contain KaRL1-8									✓

KaRL5

- KaRL5 is a list of **stakeholder-specific** requirements

→An industrial producer of TiO2 NPs is interested: *Is exposure to particles in the working environment affecting the workers lungs?*

→*What do we need to achieve KaRL5, what needs to be done?*

KaRL 5 example

Stakeholder involvement: Is exposure to particles in the working environment affecting the workers lungs?

Existing data: *in vivo* data on the effects of TiO2 on lungs from quality checked studies

(KaRLs 1-4)

Tools: Results of COmbined DOsimetry model - CoDo

estimation of the exposure levels corresponding to the concentrations *in vitro*

Occupational exposure to TiO2

New tests: *in vitro* cytotoxicity tests of TiO2 particles of interest

(by third party)

KaRL 5

Existing data: *in vivo* data on the effects of TiO2 on lungs from quality checked studies

(KaRLs 1-4)

In vitro concentration

CoDo model

Exposure concentration

1 year of inhalation
170 to 610 mg/m³

CoDo model*

100 µg/mL
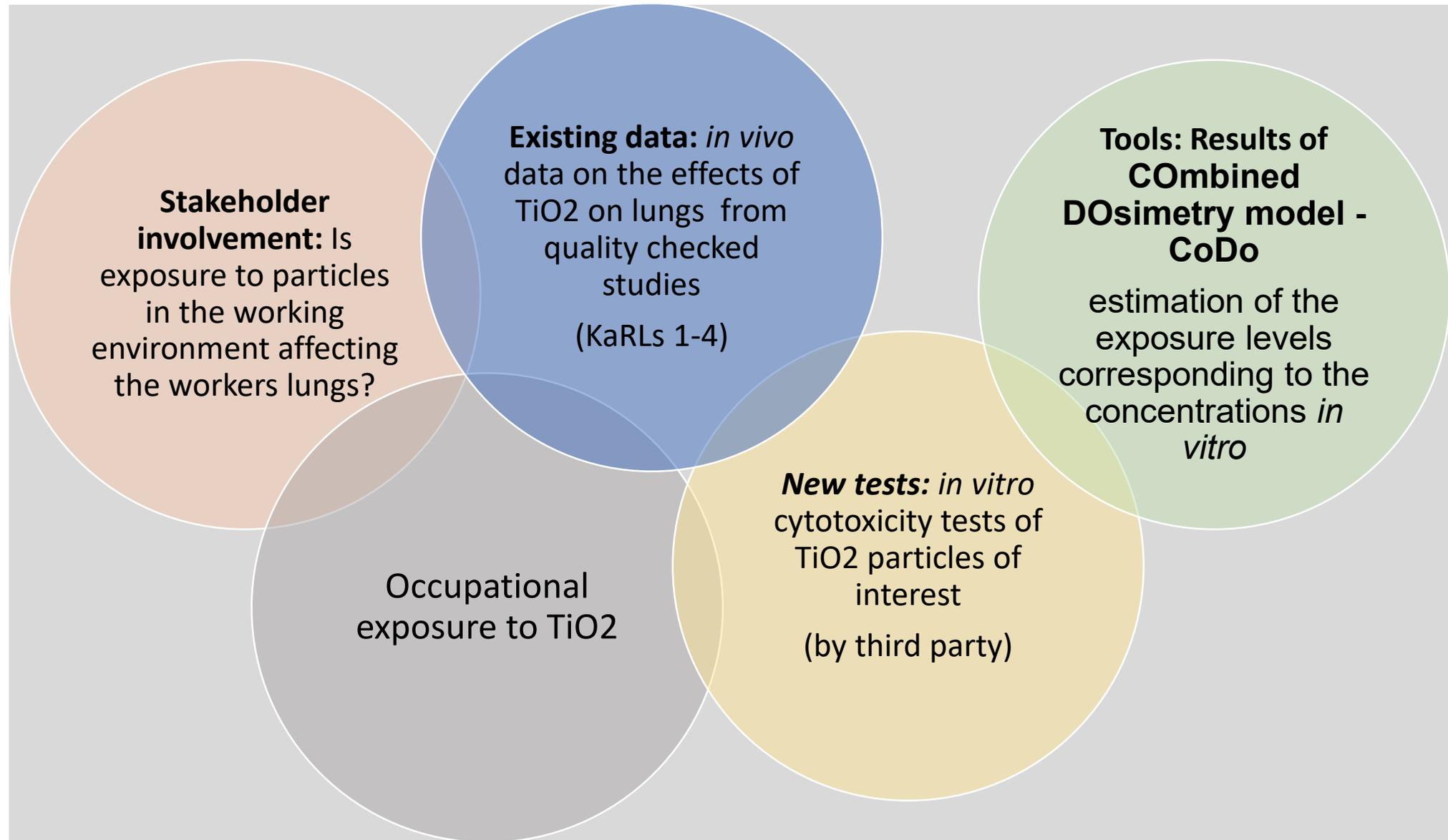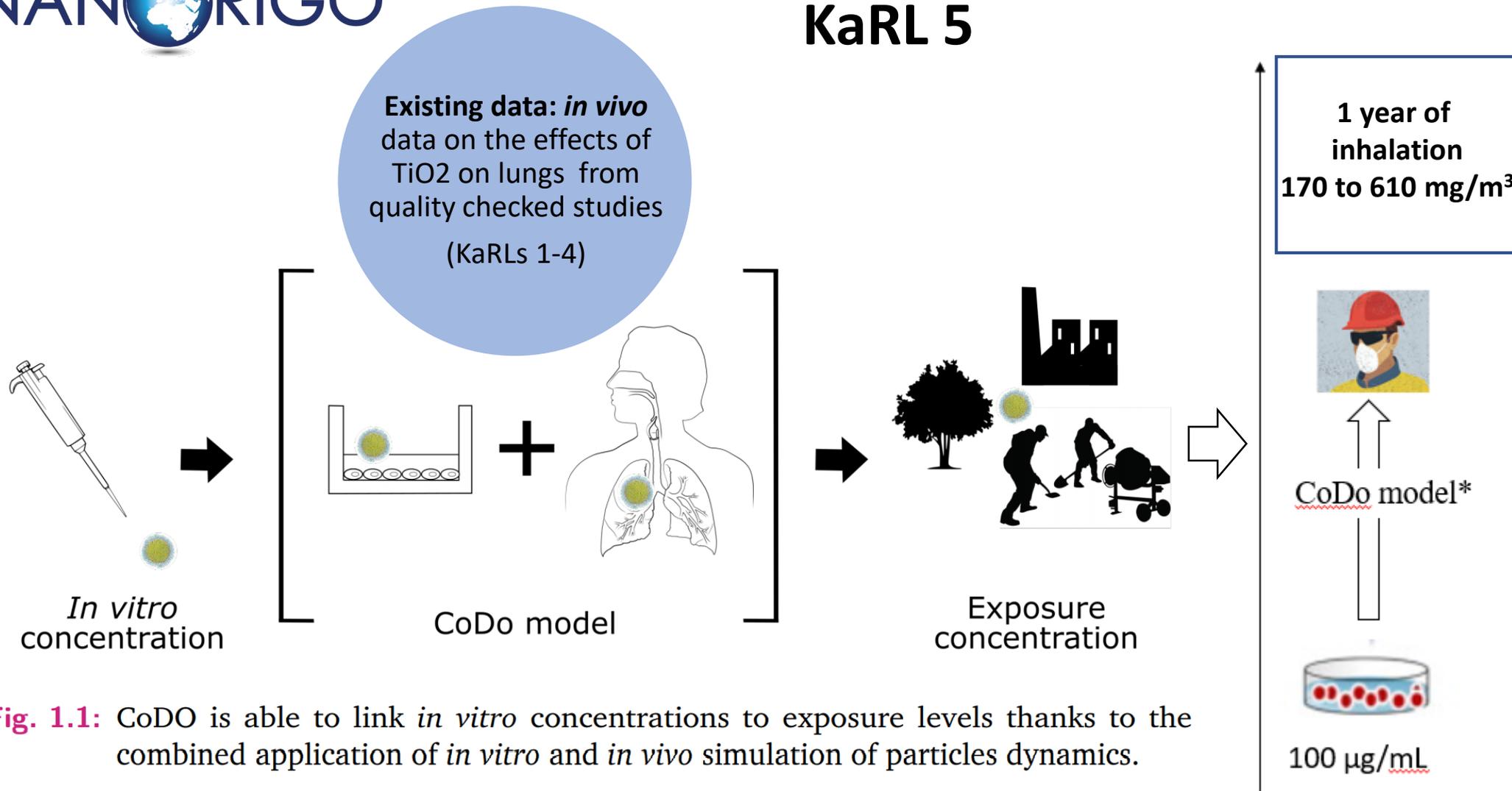
Fig. 1.1: CoDO is able to link *in vitro* concentrations to exposure levels thanks to the combined application of *in vitro* and *in vivo* simulation of particles dynamics.

In vitro tests with Nanoparticles provided by third party

KaRL6
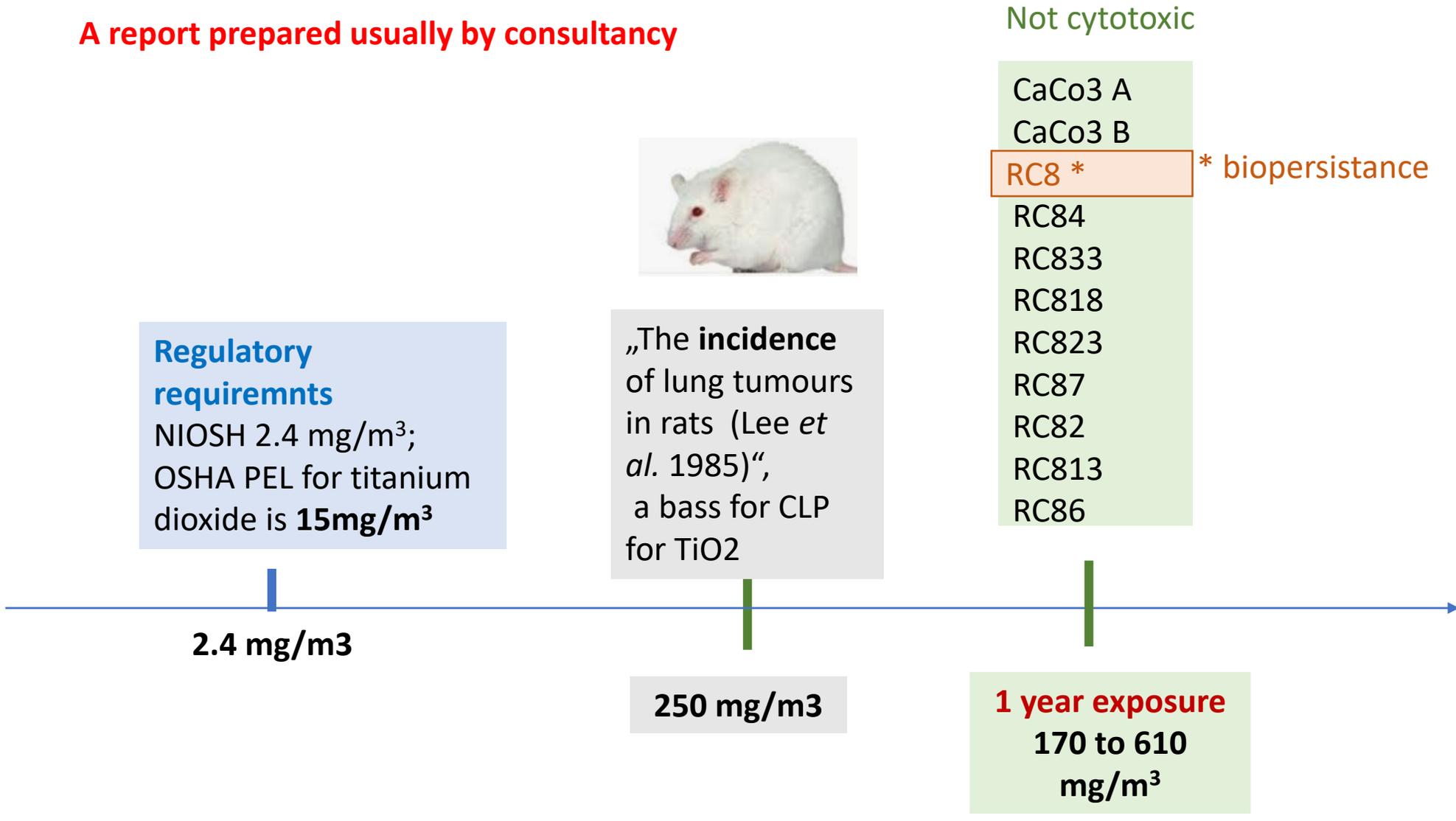
The answers to question in a form:

- a **short report**

- a **table** comparing exposure concentrations and effects

- a **scheme** showing comparison with regulatory requirements

The Answer (KaRL6) should help the company to take some additional steps to protect workers if necessary. The answer is information for producer to take action in the company and for internal communication.

KaRL 6

A report prepared usually by consultancy

Not cytotoxic

CaCo3 A
CaCo3 B
RC8 *   * biopersistance
RC84
RC833
RC818
RC823
RC87
RC82
RC813
RC86

Regulatory requiremnts
NIOSH 2.4 mg/m³;
OSHA PEL for titanium dioxide is **15mg/m³**

„The **incidence** of lung tumours in rats (Lee *et al.* 1985)",
a bass for CLP for TiO2

2.4 mg/m3

250 mg/m3

1 year exposure
170 to 610 mg/m³

An example for KaRL9 from the CLP case
Classification, Labeling and Packaging

- To fulfill KaRL9 all levels before (KaRL1-8) need to be achieved

Harmonized Classification and Labelling (CLP) classification steps

CoRap list

Putting TiO2 on a CoRap list by a member state (France)
20 March 2013

ANSES submits Proposal for (CLP) May 2016

Public consultation Comments submitted to **ECHA** (45 days) July and August 2016

ECHA's RAC committee submits opinion 9 June 2017

CARACAL meeting comments by MS 15-16 November 2017

CARACAL meeting comments by MS 7-8 March 2018

CARACAL meeting comments by MSs June, 2018 2019

Additional **public consultation** Comments submitted to **ECHA** closed on 8th Feb 2019

Decision

2020

Final decision made by **EC** February 2020

Implementation

Implementation of classification The decision goes into effect on 1 October 2021.

Could potentially be KaRL9

Legal action against the classification of TiO2 by industry 13 May 2020 (The decision of the General Court is expected to take 2 to 3 years)

2013

?