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# Air breathing organisms in risk assessment

Etje Hulzebos

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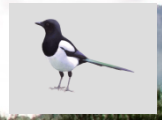
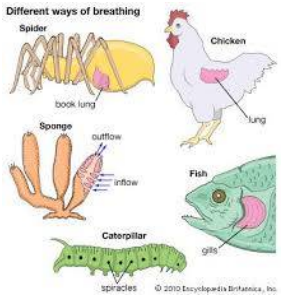


# Overview

- Goal: Finding tools to deal and handle ‘concern’ for air breathing organisms
- Regulatory framework
  - **REACH legislation**
    - Annex
    - Tonnage
  - **What is the overall target - hazard**
    - (Hazard for Air as in IUCLID chapter 6)
    - Hazard for B in PBT (vPvB)?
    - Hazard for secondary poisoning?
- **ECHA Guidance**
  - Screening versus definitive criteria
- What is the testing strategy for substances, which fulfil screening criteria
- What are the methods that can be applied
- When and how to present this information in the registration dossier

# Regulatory framework and ECHA guidance

- REACH legislation
  - In which Annex do the air breathing organism fit?
  - At which tonnage band air-breathers need assessment?
- ECHA guidance
  - Definition of organism: mammal and bird and ?
  - PBT guidance section on bioaccumulation: R11-4, pg. 68
  - What is the overall target here
    - Secondary poisoning?

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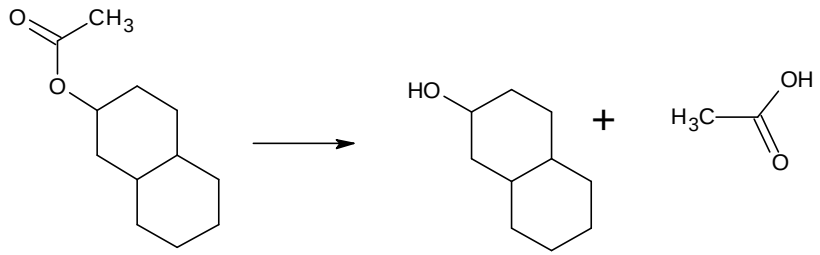
# ECHA guidance to assess the concern for air breathing organisms

- Screening criteria for the parent and its metabolite
  - Koa > 5 (EpiSuite)
  - Log Kow > 2 (Measured for the parent, calculated for the metabolite?)
- Parent
  - Koa: 5.4, Kow 3.6
  - Metabolite
    - Koa: 6.2 and Kow 2.6

De-esterification

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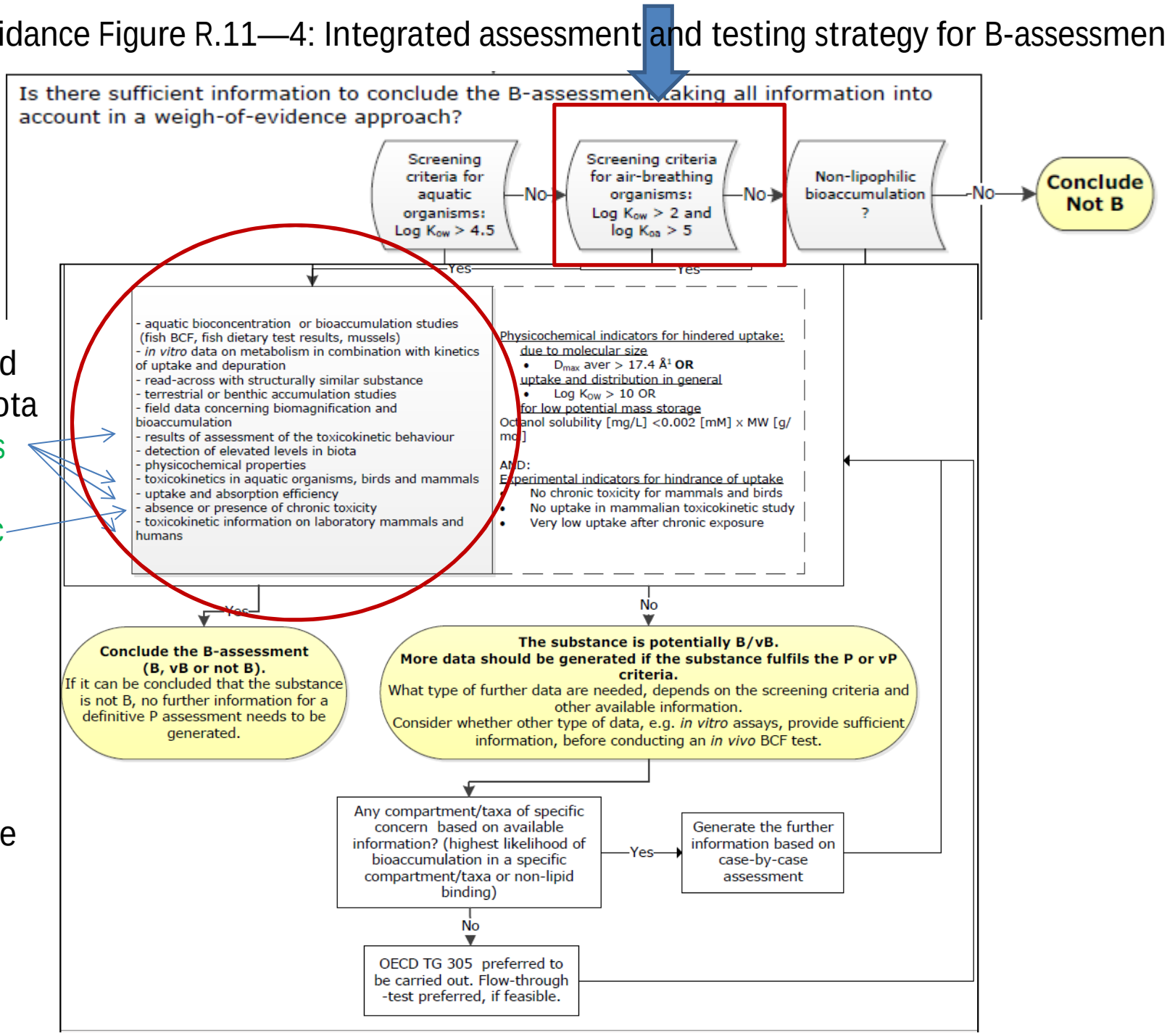
ECHA guidance Figure R.11—4: Integrated assessment and testing strategy for B-assessment.

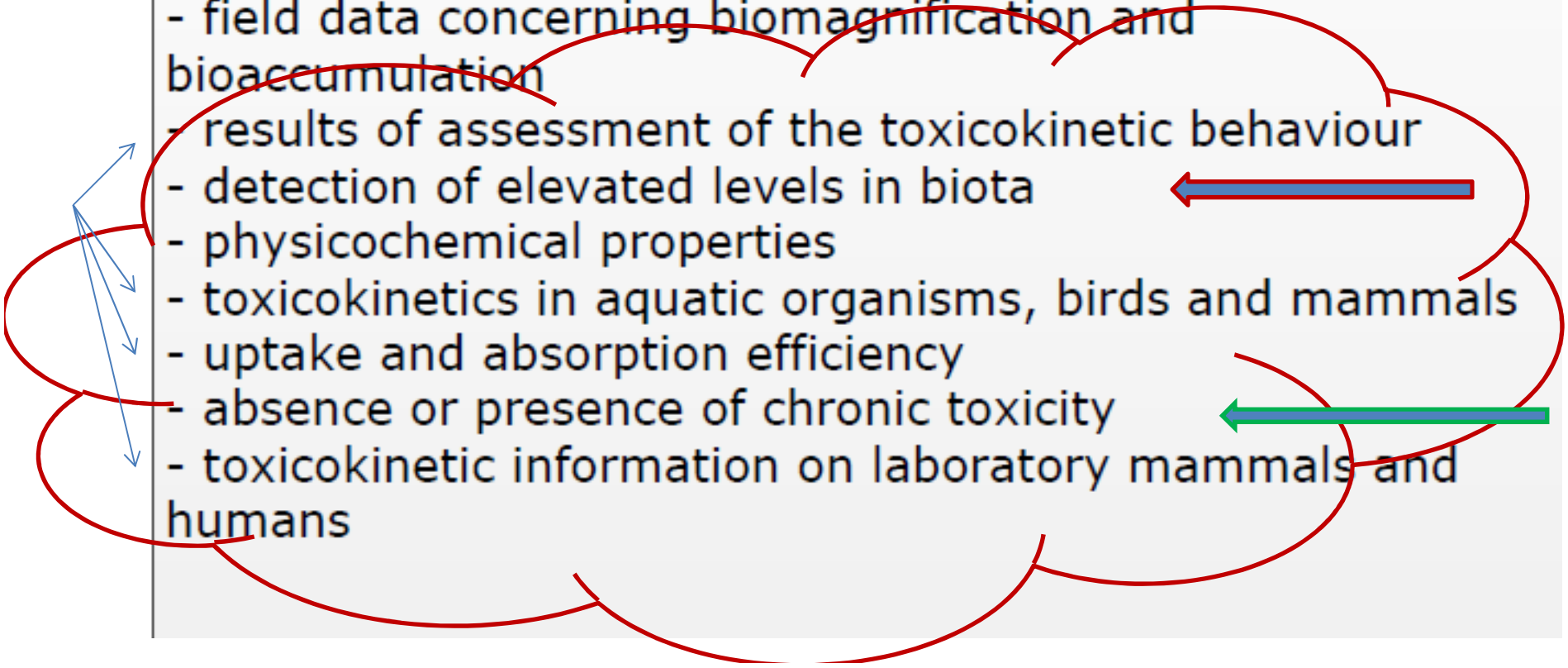



- Elevated levels biota
- Kinetics

- Chronic toxicity

Next slide

- aquatic bioconcentration or bioaccumulation studies (fish BCF, fish dietary test results, mussels)
- *in vitro* data on metabolism in combination with kinetics of uptake and depuration
- read-across with structurally similar substance
- terrestrial or benthic accumulation studies
- field data concerning biomagnification and bioaccumulation
- results of assessment of the toxicokinetic behaviour
- detection of elevated levels in biota
- physicochemical properties
- toxicokinetics in aquatic organisms, birds and mammals
- uptake and absorption efficiency
- absence or presence of chronic toxicity
- toxicokinetic information on laboratory mammals and humans



# Definitive criteria to assess concern for air-breathers

- Include kinetic information?
  - Can this be theoretical
  - Should this be experimental
- Chronic toxicity: T criteria
  - Secondary poisoning criteria?

# Testing strategy after fulfilling screening criteria

- Refine the calculated Koa by measuring this value
- Use other QSAR: Blood-air partition coefficient of Buist et al.
- **ECHA guidance**
  - **Chronic toxicity studies with mammals – this first?**
    - If chronic toxicity studies with mammals are available, the complete absence of effects in the long-term is an indication that the compound is either chronically non-toxic and/or that it is not taken up to a significant extent. Although this is only indirect information on the uptake of a substance, it may be used together with other indicators, e.g. referring to non-testing information, to conclude in a **Weight-of-Evidence approach that a substance is likely to be not B or vB.**
  - **Toxicokinetic studies with mammals – this second?**
    - **Theoretical or experimental**
- **Does this sufficiently cover other (vertebrate) air breathing organism**

# Reach framework Summary and IUCLID fill

- REACH legislation
  - Where do the air breathing organism fit?
  - When to assess?
  - Annex XIII?
  - Hazard for predators?
- ECHA guidance
  - Bioaccumulation – PBT assessment in B section?
    - Direct versus indirect exposure
  - There is a lot of WoE: how and where to present?
- IUCLID
  - Overall Endpoint summary: Chapter 4 Fate assessment?
  - Reference to
    - Bioaccumulation study
    - Kinetic records and/or Endpoint summaries
    - Chronic mammalian toxicity?

# Dank voor uw aandacht

Etje Hulzebos – IFF Hilversum
etje.hulzebos@iff.com

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