GMO Feeding Studies and Rodent Cancer Bioassays

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PETA INTERNATIONAL SCIENCE CONSORTIUM LTD.

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PETA International Science Consortium Ltd.

Promote reliable, relevant non-animal testing methods

Fund and organise method development and validation efforts

Promote international acceptance of non-animal methods

Provide regulatory staff with training opportunities

Conduct retrospective analyses

Organise and participate in workshops and webinars

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Overview

The PETA International Science Consortium

Rodent Cancer Bioassays

GMO Feeding Studies

Rodent cancer bioassay background

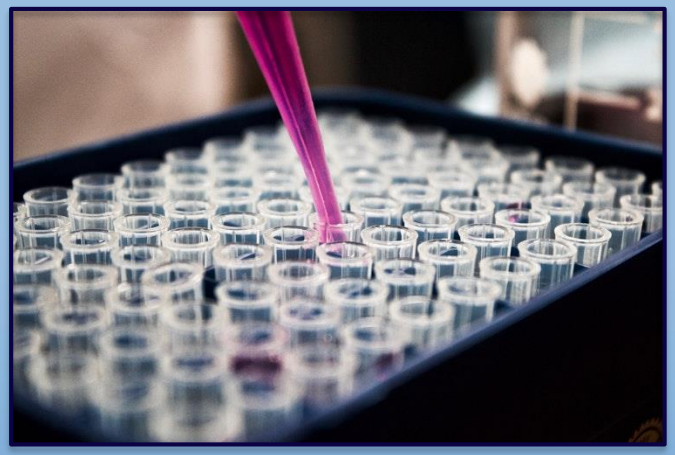
- **Glyphosate debate + EU reauthorisation in 2017**
- **European Parliament's Special Committee on the European Union's authorisation procedure for pesticides (PEST)**
- **Regulation (EU) 283/2013 setting out data requirements for pesticide active ingredient (AI)**
- **Rat bioassay is required; mouse bioassay can be waived**
- **400 animals per test. Multiple tests per AI.**

Rodent cancer bioassay background

- **Why are validation standards important?**
  - **Reliable**
  - **Reproducible**
  - **Relevant**
- **Rodent studies are poorly reproducible.**
- **Glyphosate: 14 rodent cancer bioassay = 3,500 animals. No reproducible results. Low concordance**
- **Human carcinogens ≠ Rat carcinogens**

Non-animal methods

Assessing chemical carcinogenicity is complex, but scientists are rapidly establishing new strategies for identifying potential human carcinogens.



- **Carcinogen screening: using human tissues**
- **Carcinogenic chemical signatures: advanced computational models**
- **Long-term human population studies: collecting decades of data - correlation between pesticide application and cancer.**

The focus must be on human-relevant data.

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GMO Feeding Studies

GMO feeding studies requirements

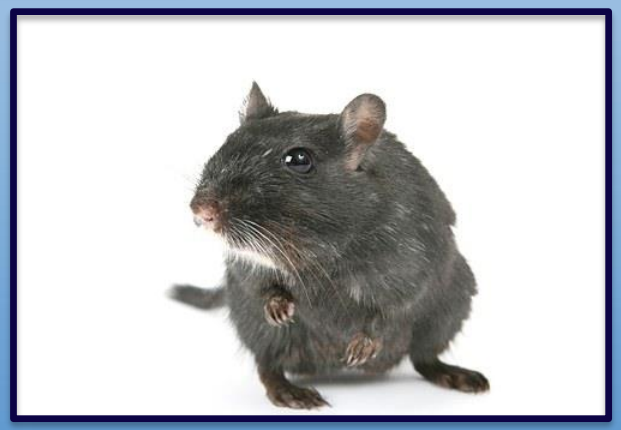
Commission Implementing Regulation (EU) 503/2013

28-day repeated-dose study using rodents required for newly expressed proteins

90-day feeding study using rodents required for whole GM food/feed product

GMO 90-day feeding study

- **Used to characterize gene-influencing alterations in the food/feed matrix**
- **No formal guideline so OECD 408 was adapted to a comparative limit-test design with *no hypothesis to test***
- **Roughly 80 rats/mice per study**



GMO feeding studies provide “little additional value”

“where molecular, compositional, phenotypic, agronomic and other analyses have demonstrated equivalence between the GM plant and derived food and feed and its comparator, … the performance of animal feeding trials with rodents or other (target) animal species (e.g. broilers) is of little additional value if any, and is therefore not deemed necessary on a routine basis.”

EFSA Panel on Genetically Modified Organisms. Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011; 9(5):2150

Lack of sensitivity

"This subchronic testing paradigm has been applied to the safety assessment of food and feed from GM crops for over a decade with **no evidence of adverse effects reported to date**."

Safety Assessment of Food and Feed from GM Crops in Europe: Evaluating EFSA's Alternative Framework for the Rat 90-day Feeding Study 2017

Do we need the 90-day feeding study?

Recital 12: “The **current uncertainties** in relation to **the need** and design of 90-day feeding trials will be addressed by a large research project under the 2012 work programme of Theme 2 ‘Food, Agriculture and Fisheries, and Biotechnologies’ of the seventh Framework Programme for Research (FP7). ”

Commission Implementing Regulation EU 503/2013

Assessing short- and long-term feeding studies

GRACE and G-TWySST studies

"[a]nimal feeding studies **add limited value** to GM plant risk assessment"

"**[n]o health risks**, including no carcinogenicity, were found for the GM maize tested"

"[t]he mandatory requirement to conduct untargeted animal feeding studies for each novel GM plant **should be discontinued**."

GMO Risk Assessment and Communication of Evidence. Animal feeding studies add limited value to GM Plant risk assessment. http://www.grace-fp7.eu/en/content/animal-feeding-studies-add-limited-value-gm-plant-risk-assessment. Published June 6, 2018.

MS and Commission decision: does it make sense?

"…[T]he Commission considers it is appropriate to **maintain the requirement for the submission of a 90-day oral toxicity study in rodents** for each single GM event as part of the application data package..."

"The requirement for the 90-day oral toxicity study will be **reviewed in the future** in light of progress made in the development of validated in vitro methods."

European Commission. Review of the requirement to perform 90-day feeding studies in rodents. 2017

MS and Commission decision: does it make sense?

Feeding studies are required in every assessment, not case-by-case.

Contradicts **Directive 2010/63/EU to minimize the use of animals in research**

Regulators must accept tiered strategies that test specific risk hypotheses.

Points for discussion

Rodent cancer bioassay:

- How often is testing on two species carried out, and what is the added value?
- What do risk assessors need in order to replace this test?
- Would risk assessors consider waivers containing subchronic and mechanistic data in place of the rodent cancer bioassay?

GMO feeding studies:

- What action is being taken following publication of the GRACE and G-TWyST studies?
- When will changes to animal test requirements be proposed?

Thank you for listening!

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