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THE SCIENTIFIC RATIONALE BEHIND 90-DAY FEEDING TRIAL REQUESTS

GMO NETWORK REPRESENTATIVES' PERSPECTIVES

EFSA GMO SCIENTIFIC NETWORK MEETING 18-19 June 2019

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WHY?

TO INFORM YOU WHERE WE ARE WITH THIS TOPIC

TO SEE HOW GRACE & G-TwYST HAS INFLUENCED THE OPINION OF GMO NETWORK REPRESENTATIVES

TO INCREASE MUTUAL UNDERSTANDING ON THE SCIENTIFIC NEED OF A 90-DAY FEEDING TRIAL

TO SHARE INFORMATION

OVERVIEW

1. **Background & overview of outcomes of GRACE, G-TwYST, GMO 90+**

   Gijs Kleter

2. **Overview of GMO Network perspectives**

   Adinda De Schrijver

3. **Tour de Table - Q&A - Discussion**

   everyone

4. **rap-up**

OUTCOMES EU & FRENCH PROJECTS

THREE MUTUALLY LINKED PROJECTS:

- **GRACE (EU)**
  - FEEDING TRIALS, DESK RESEARCH, IN-VITRO TOX & OMICS, CROP OMICS, CADIMA DATABASE
  - EU, 2012-2015, 7.8 M€, 19 PARTNERS, COORDINATOR JULIUS KÜHN INSTITUTE
  - REFERRED TO BY IMPLEMENTING REGULATION
- **G-TWYST (EU)**
  - FEEDING TRIALS, CROP OMICS
  - 2014-2018, 3.8 M€, 9 PARTNERS, COORDINATOR VETERINARY UNIVERSITY HANNOVER
- **GMO90+ (FR)**
  - FEEDING TRIALS, TOX-METABONOMICS, CROP ANALYSIS
  - 2014-2018, 3.7 M€, 10 PARTNERS, COORDINATOR TOXALIM
- *ALSO LINKAGES WITH OTHER PROJECTS, E.G. MARLON, PRESTO, AMIGA*
- *STAKEHOLDER INVOLVEMENT = IMPORTANT COMPONENT, E.G. WORKSHOPS, CONSULTATIONS*

OUTCOMES EU & FRENCH PROJECTS

GRACE
GMO Risk Assessment and Communication of Evidence

G-TwYST
GM PLANTS TWO YEAR SAFETY TESTING

GM90+

Joint GRACE & G-TwYST recommendations (examples)

- Rat feeding studies with whole food/feed
  - Scientific value:
    - Chronic tests confirmed initial data and 90-d tests (no adverse effects)
    - No added value of adding immune function parameters to 90-d test
    - Necessity to perform a feeding trial should be carefully evaluated
      - *N.B. GMO90+ concurs: Value of the 90-day rodent study is limited without a specific hypothesis; it will not reduce scientific uncertainties*
- Design, conduct and analyses
  - E.g. number of animals *vs.* statistical power, historic references
  - Usefulness of patterns (instead of single endpoints) within chronic test results
- Compositional analysis (e.g. quality control)

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OUTCOMES EU & FRENCH PROJECTS

GRACE:

- OBJECTIVES
  - INFORMATION PROVISION (REVIEWS, 1-STOP SHOP), DATA GAPS, ASSESSMENT OF ADDED VALUE OF FEEDING TRIALS
- FEEDING TRIALS
  - MAIZE MON810 (GM, 2X), CONTROL, REFERENCE LINES
  - 90-DAY & 1-YEAR, 0-11-33% INCLUSION RATE
  - ACCORDING TO EFSA & OECD GUIDELINES
- ADDITIONAL OMICS ANALYSES ON ANIMAL AND PLANT MATERIALS
- IN-VITRO TOXICITY TESTING
- WEBSITE HTTP://WWW.GRACE-FP7.EU/

OUTCOMES EU & FRENCH PROJECTS

GRACE:

- **OUTCOMES**
  - **FEEDING TRIALS: NO ADVERSE EFFECTS OBSERVED**
    - **VARIOUS DIFFERENCES OBSERVED WERE UNRELATED TO MON810**
  - **IN-VITRO TOX: NO EFFECTS OF MON810**
    - **E.G. EFFECTS OF CIRCADIAN RHYTHM DETECTED**
  - **CROP OMICS: NO IMPACTS OF GM (OTHER FACTORS INFLUENTIAL)**
  - **REVIEW/MAPPING OF EVIDENCE: NO NEW DATA IMPACTING ON FINDINGS**
- **RECOMMENDATIONS PUBLISHED JOINTLY WITH G-TWYST**

OUTCOMES EU & FRENCH PROJECTS

G-TwYST:

- FEEDING TRIALS
  - NK603 MAIZE, TREATED/UNTREATED WITH GLYPHOSATE; & CONTROL
  - INCLUSION RATE 0-11-33% (PLUS 50% IN EXTRA 90-D TRIALS)
  - SUB-CHRONIC 90-DAY, CHRONIC 1-YEAR AND CARCINOGENICITY (2-YEAR)
- ADDITIONAL ANALYSES
  - CROP COMPOSITION & OMICS
  - ADDITIONAL CONSIDERATIONS, *E.G.*, STATISTICS, INPUTS FROM LITERATURE, POINTS TO CONSIDER FOR DESIGN AND EXECUTION OF ANIMAL FEEDING TRIALS
- OUTCOMES
  - FEEDING TRIALS: NO ADVERSE EFFECTS OBSERVED
  - RECOMMENDATIONS ON JUSTIFICATION AND SCIENTIFIC VALUE
    - STUDIES PERFORMED IN ABSENCE OF HYPOTHESIS
    - NO BASIS FOR 90-DAY FEEDING TRIALS PROVIDED BY GRACE AND G-TWYST
    - NO VALUE OF EXTENSION TO LONG-TERM TRIALS
  - RECOMMENDATIONS DOCUMENT PUBLISHED JOINTLY WITH GRACE
- WEBSITE: HTTPS://WWW.G-TWYST.EU/

OUTCOMES EU & FRENCH PROJECTS

GMO90+:

- **Feeding trials**
  - **NK603 and MON810 maize; & control**
  - **Inclusion rate 0-11-33%**
  - **Subchronic 90-day, chronic 0.5-year**
- **Additional analyses:**
  - **Tissue omics (metabolomics on fluids, transcriptomics on liver & kidney)**
  - **Crop composition & omics**
- **Outcomes**
  - **Feeding trials: No adverse effects observed related to GM nature**
    - **Few differences observed could not be linked to absence of effects in biologically linked variables**
    - **Effects of maize variety and location of cultivation**
    - **No biomarker identified attributable to health effects of GMOs**
- **Website: http://recherche-riskogm.fr/en/page/gmo90plus**

GMO NETWORK PERSPECTIVES

Scientific perspective on:

- 90-day feeding trials for single events
- (Re-)assessment of single events at the level of the 90-day feeding trial in the context of GM stacked events

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QUESTIONNAIRE

1. Do you consider a 90-day feeding trial is only relevant on a case-by-case basis when a clear hypothesis for testing can be formulated? If not:

   1a. Please provide your scientific rationale for asking a 90-day feeding study for every application.

   1b. Did the outcome of the GRACE & G-TwYST project impact your point of view? Please explain briefly why this did or did not.

2. Do you consider that 90-day studies for single events previously positively assessed by EFSA, need to be re-assessed/re-conducted in the context of GM stacked events?

OUTCOME CONSULTATION

1. Do you consider a 90-day feeding trial is only relevant on a case-by-case basis when a clear hypothesis for testing can be formulated?

YES: GMO Network representatives from 20 European countries

NO: GMO Network representatives from 5 European countries

?: GMO Network representatives from 6 European countries

2. Do you consider that 90-day studies for single events previously positively assessed by EFSA, need to be re-assessed/re-conducted in the context of GM stacked events?

YES: -

NO: GMO Network representatives from 21 European countries

OUTCOME CONSULTATION

1a. Please provide your scientific rationale for asking a 90-day feeding study for every application.

Reply: *90-day feeding trial can provide answers*

Reply: *due to the limited number of compounds tested during compositional assessment, identification of unintended effects is not always possible. This uncertainty may be overcome by a 90-day feeding trial.*

1b. Did the outcome of the GRACE & G-TwYST project impact your point of view? Please explain briefly why this did or did not.

Reply: *outcome of GRACE & G-TwYST does not allow to go for case-by-case, as a feeding trial with one GM crop is not sufficient to conclude what can happen with another*

Reply: *GRACE project did not due to inadequacies in final report*

Tour de Table - Q&A - Discussion

Q & A

RAP-UP

“ 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 … FP7 … The requirements … should be reviewed in the light of this project …(IR 503/2013)”