INFORMATION and NETWORKING EVENT
organised by
DG RTD, the NCPs for HEALTH, and Colipa

16 November 2009 in Brussels

FP7 HEALTH-2010 – Area 4.2-9: Towards the replacement of repeated dose systemic toxicity testing in human safety assessment

European Commission DG RTD.F.5, Health Biotechnology / Juergen Buesing

1

Title of the Call:

HEALTH.2010.4.2-9: Towards the replacement of repeated dose systemic toxicity testing in human safety assessment

Call identifier:
FP7-HEALTH-2010-Alternative Testing Strategies
Opening date of call: 30 July 2009
Closing date of call: 3 February 2010
EU contribution: up to EUR 25 million

Colipa commitment: to fund the projects selected by the EC with the same amount (up to EUR 25 million)

Expected duration of projects: 5 Years for Integrating Projects; 6 years for Coordinating Action

Not legally binding

2

For scientific and administrative management reasons the research topic has been broken down into six complementary inter-connected Integrating Projects.

Six Integrating Projects: -> scientific foundation to develop strategies for the replacement of repeated dose systemic toxicity testing

Co-ordinating Action:
Organisation of experts meetings, workshops, symposia; tailor-made reporting; identification of knowledge gaps and respective RTD needs and priorities, …

Funding scheme:
EC contribution 50% of eligible costs – grant agreement with EC
Remaining 50% covered by cosmetics industry – research agreement with Colipa

Not legally binding

3

Topics of Integrating Projects:

4.2.9.1 Optimisation of current methodologies and development of novel methods to achieve functional differentiation of human-based target cells in vitro
EUR 4 000 000 – EUR 5 000 000

4.2.9.2 Exploitation of organ-simulating cellular devices as alternatives for long-term toxicity testing
EUR 4 000 000 – EUR 5 000 000

4.2.9.3 Establishment of endpoints and intermediate markers in human-based target cells with relevance for repeated dose systemic toxicity testing
EUR 3 500 000 – EUR 4 500 000

Not legally binding

4

Topics of Integrating Projects (cont.):

4.2.9.4 Computational modelling and estimation techniques
EUR 2 500 000 – EUR 3 500 000

4.2.9.5 Systems biology for the development of predictive causal computer models
EUR 4 000 000 – EUR 5 000 000

4.2.9.6 Integrated data analysis and servicing
EUR 2 000 000 – EUR 3 000 000

4.2.9.7 Coordination action
Max EUR 1 500 000

Not legally binding

5

Research Cluster

Organ-simulating Cellular Devices
- Integration of human-based target cells
- Utilisation of scaffolds and microstructures
- Development of novel cellular barrier models
- Optimisation of microsensors

Human-based Target Cells
- Optimisation of stem cell technology
- Refinement of existing cell culture systems
- Development of innovatice cell culture techniques

Integrated Data Analysis and Servicing
- Dedicated web-based data warehouse
- Database of selected model compounds
- Depository of selected model compounds
- Cell and tissue bank for *in vitro* toxicity testing

HUMAN SAFETY ASSESSMENT STRATEGIES

Endpoints and Intermediate Markers
- Functional parameters
- "-Omics"-based markers
- Integration of markers

Computational Modelling and Estimation Techniques
- Application of TTC approach
- Development of innovative computational chemistry approaches
- Development of kinetic modelling (effective concentration)
- Application of PBPK modelling (ADME)

Systems Biology
- Pathway analysis by genetic tools
- Development of causal predictive computer models
- Use of "-omics"-based techniques

6

Sub-topics of Integrating Projects:

4.2.9.1 Optimisation of current methodologies...

a) Optimisation of stem cell technology as a source for human-based target cells for toxicological purposes

b) Refinement of cell culture systems for long-term toxicity testing

c) Exploitation of emerging mechanistically-driven methods controlling cellular differentiation

Not legally binding

7

Sub-topics of Integrating Projects (cont.):

4.2.9.2 Exploitation of organ simulating cellular devices...

a) Integration of target and metabolising cells to simulate multi-organ-related toxicity in vitro

b) Utilisation of scaffolds and microstructures to optimise the cellular micro-environment

c) Development of novel cellular barrier models relevant to systemic exposure

d) Optimisation of micro-sensors to monitor tissue responses in organ-simulating devices

Not legally binding

8

Sub-topics of Integrating Projects (cont.):

4.2.9.3 Establishment of endpoints...

a) Functional parameters as predictive signals of human long-term toxicity

b) Establishment of "-omics"-based markers as predictive signals of human long-term toxicity

c) Integration of markers for enhancement of human long-term predictive capacity

Not legally binding

9

Sub-topics of Integrating Projects (cont.):

4.2.9.4 Computational modelling...

a) Threshold of toxicological concern approach for the safety assessment of cosmetic ingredients

b) Innovative computational chemistry approaches in the safety assessment of cosmetic ingredients

c) Predicting the dose at target level upon long-term exposure

d) PBPK modelling in the safety assessment of cosmetic ingredients

Not legally binding

10

Sub-topics of Integrating Projects (cont.):

4.2.9.5 Systems biology...

a) Identification and analysis of pathways relevant to long-term toxicity by genetic tools

b) Use of "-omics"-based techniques to identify mechanistic pathways involved in long-term toxicity effects

c) Development of causal predictive computer models for long-term toxicity effects

Not legally binding

11

Sub-topics of Integrating Projects (cont.):

4.2.9.6 Integrated data analysis and servicing

a) Establishment of a dedicated web-based "data warehouse"

b) Establishment of a database of selected model compounds

c) Establishment of a repository for the selected model compounds

d) Setting up a cell and tissue bank for in vitro toxicity testing

Not legally binding

12

FP7 – Area 4.2-9
Toward the replacement of repeated dose systemic toxicity testing in human safety assessment

Specific conditions

- No tests on living animals
- Nanoparticles excluded

- Each proposal submitted in one of the six topics has to clearly describe the interconnections and interfaces with the other five topics.

- The partners in all research projects selected for funding should agree to an integrated data analysis concept.

Not legally binding

13

Detailed information available at:

http://www.cordis.europa.eu/

http://www.colipa.eu/

Background information:

EPAA: http://ec.europa.eu/enterprise/epaa/index_en.htm

Alternative Testing Strategies/ Progress Report 2009 on EU projects:
http://cordis.europa.eu/documents/documentlibrary/106691831EN6.pdf

14

Interactions between projects (1)

- **Projects 4.2.9.1 – 4.2.9.5 send data into the « data warehouse » of 4.2.9.6**
- **Project 4.2.9.6 shall send results of the analysis of the data received to projects 4.2.9.1 – 4.2.9.5**
- **Strong cooperation between 4.2.9.6 and the other projects concerning (virtuell) cell and tissue banking**
- **Strong cooperation between 4.2.9.6 and the other projects on the selection and management of (reference) chemicals**

Not legally binding

15

Interactions between projects (2)

- **Organisation of cluster meetings, tailor-made reporting, gap analysis, definition of research priorities etc. will be handled by the scientific secretariat (project 4.2.9.7) or coordination project with the help of an 'experts group'.**
- **The coordination action shall provide the necessary infrastructure for this approach. The scientific secretariat should be kept as efficient as possible and should guarantee continuity over the life time of the research cluster.**

Not legally binding

16

Practical hints (1)

- Read, understand and discuss <u>all</u> topics of the call on « alternative testing strategies ».
- Clearly position your proposal in this research area.
- Draw 'operational lines' between the subtopics of your proposal and those of the other research topics indicating interfaces for cooperation.
- Indicate clearly the borderlines of your proposal.
- Keep in mind the overall goals of the research cluster: the development of a strategy « towards the replacement of repeated dose systemic toxicity testing ».

Not legally binding

17

Practical hints (2):

- Cross-check proposal with « expected impacts »:
- ***<u>Expected overall impacts:</u>***
- ***« Significant contribution to the development of safety testing methods with higher predictive value, faster and cheaper than animal tests; significant reduction of animals currently used in safety testing. »***
- Important: Read carefully the « expected impact » of the individual projects! Distinguish between long-term expectations and short-term impacts!
- Read the Progress Report 2009 on « Alternative Testing Strategies »

Not legally binding

18