Directive 2010/63/EU

Moving transparency to the next level – Non-technical project summaries under the Directive

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Susanna Louhimies
DG Environment, European Commission

Moving transparency to the next level – to the service of Reduction and Refinement

- *Transparency in the Directive*
- *2013 - 2019*
- *Transparency in the service of Reduction and Refinement*

Why is transparency needed?

- *Compliance and accountability*
- *Societal acceptance through demonstration of adherence to societal values*
- *Trust building*
- *Factual data as basis for policies and decision making*

Transparency in the Directive

Tools and obligations in the Directive, *inter alia*

1. *Non-technical project summaries (NTS)*
2. *Revised statistical reporting on animal use*

1. The Directive and Non-technical project summaries

- *Objectives*
- *Predicted harms (incl. # and types of animals)*
- *Expected benefits*
- *<u>Demonstration</u> of **compliance with** the requirement of **the Three Rs***

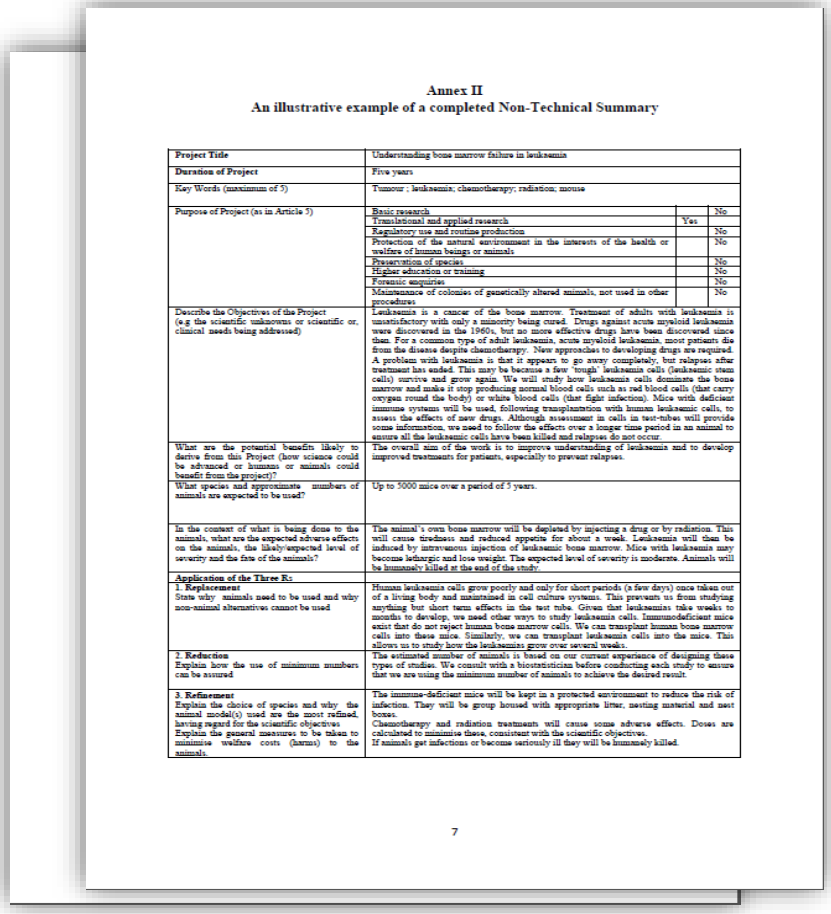
1. The Directive and Retrospective Assessment

- *Whether **objectives** were **achieved***
- ***Actual harms**, including # and **species** of animals used, and the **severities** of the procedures, and*
- *Any elements that may contribute to the **further implementation** of **the Three Rs***

1. Non-technical project summaries

- *In 2013, a **template** and an **illustrative example** agreed at the EU level*

http://ec.europa.eu/environment/chemicals/lab_animals/interpretation_en.htm



Annex II
An illustrative example of a completed Non-Technical Summary

Project Title	Understanding bone marrow failure in leuksemia		
Duration of Project	Five years		
Key Words (maximum of 5)	Tumour ; leuksemia; chemotherapy; radiation; mouse		
Purpose of Project (as in Article 5)	Basic research		No
	Translational and applied research	Yes	
	Regulatory use and routine production		No
	Protection of the natural environment in the interests of the health or welfare of human beings or animals		No
	Preservation of species		No
	Higher education or training		No
	Forensic enquiries		No
	Maintenance of colonies of genetically altered animals, not used in other procedures		No
Describe the Objectives of the Project (e.g the scientific unknowns or scientific or, clinical needs being addressed)	Leuksemia is a cancer of the bone marrow. Treatment of adults with leuksemia is unsatisfactory with only a minority being cured. Drugs against acute myeloid leuksemia were discovered in the 1960s, but no more effective drugs have been discovered since then. For a common type of adult leuksemia, acute myeloid leuksemia, most patients die from the disease despite chemotherapy. New approaches to developing drugs are required. A problem with leuksemia is that it appears to go away completely, but relapses after treatment has ended. This may be because a few 'tough' leuksemia cells (leuksemic stem cells) survive and grow again. We will study how leuksemia cells dominate the bone marrow and make it stop producing normal blood cells such as red blood cells (that carry oxygen round the body) or white blood cells (that fight infection). Mice with deficient immune systems will be used, following transplantation with human leuksemic cells, to assess the effects of new drugs. Although assessment in cells in test-tubes will provide some information, we need to follow the effects over a longer time period in an animal to ensure all the leuksemic cells have been killed and relapses do not occur.		
What are the potential benefits likely to derive from this Project (how science could be advanced or humans or animals could benefit from the project)?	The overall aim of the work is to improve understanding of leuksemia and to develop improved treatments for patients, especially to prevent relapses.		
What species and approximate numbers of animals are expected to be used?	Up to 5000 mice over a period of 5 years.		
In the context of what is being done to the animals, what are the expected adverse effects on the animals, the likely/expected level of severity and the fate of the animals?	The animal's own bone marrow will be depleted by injecting a drug or by radiation. This will cause tiredness and reduced appetite for about a week. Leuksemia will then be induced by intravenous injection of leuksemic bone marrow. Mice with leuksemia may become lethargic and lose weight. The expected level of severity is moderate. Animals will be humanely killed at the end of the study.		
Application of the Three Rs			
1. Replacement State why animals need to be used and why non-animal alternatives cannot be used	Human leuksemia cells grow poorly and only for short periods (a few days) once taken out of a living body and maintained in cell culture systems. This prevents us from studying anything but short term effects in the test tube. Given that leuksemias take weeks to months to develop, we need other ways to study leuksemia cells. Immunodeficient mice exist that do not reject human bone marrow cells. We can transplant human bone marrow cells into these mice. Similarly, we can transplant leuksemia cells into the mice. This allows us to study how the leuksemias grow over several weeks.		
2. Reduction Explain how the use of minimum numbers can be assured	The estimated number of animals is based on our current experience of designing these types of studies. We consult with a biostatistician before conducting each study to ensure that we are using the minimum number of animals to achieve the desired result.		
3. Refinement Explain the choice of species and why the animal model(s) used are the most refined, having regard for the scientific objectives Explain the general measures to be taken to minimise welfare costs (harms) to the animals.	The immune-deficient mice will be kept in a protected environment to reduce the risk of infection. They will be group housed with appropriate litter, nesting material and nest boxes. Chemotherapy and radiation treatments will cause some adverse effects. Doses are calculated to minimise these, consistent with the scientific objectives. If animals get infections or become seriously ill they will be humanely killed.		

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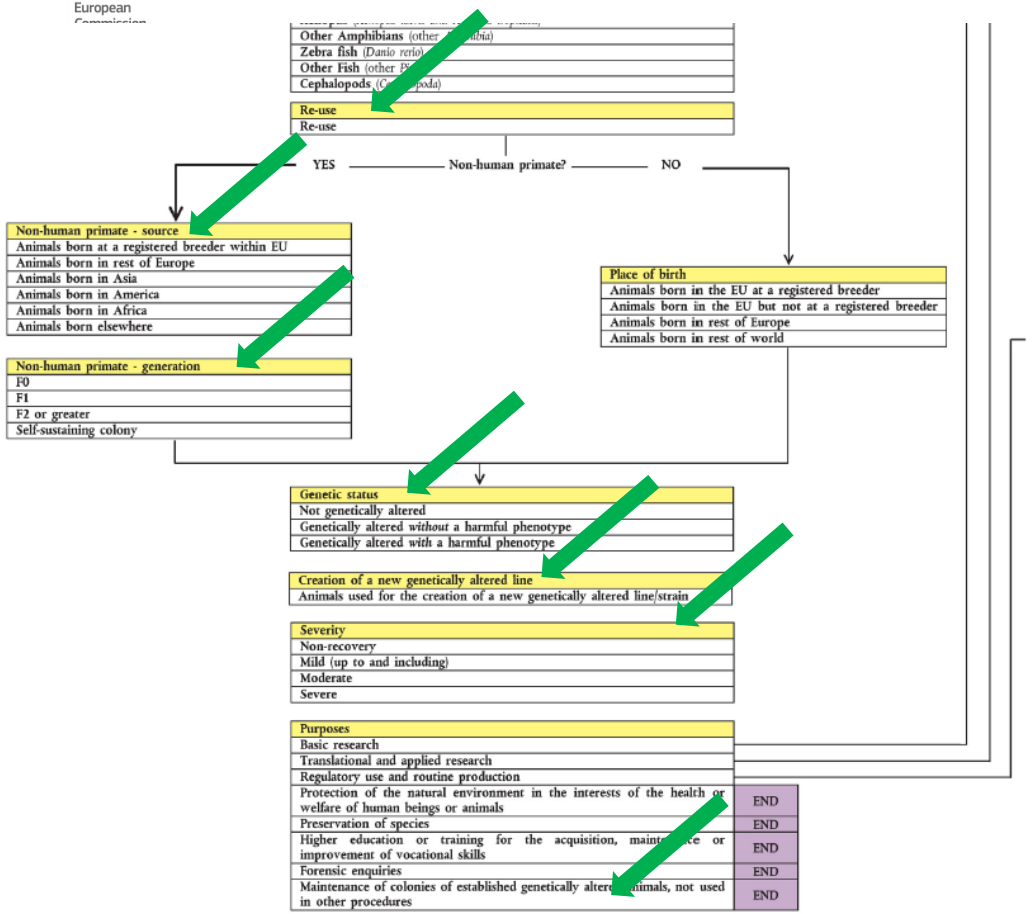
2. Key changes in statistical reporting in the EU

- ***The scope:*** *cephalopods, creation and maintenance of genetically altered animals*
- ***Each use counted:*** *allows data on numbers of "animals" and details of "all uses"*
- ***Time of reporting*** *at the end of each use*
- ***Actual severity*** *experienced by each animal*

2. Key changes



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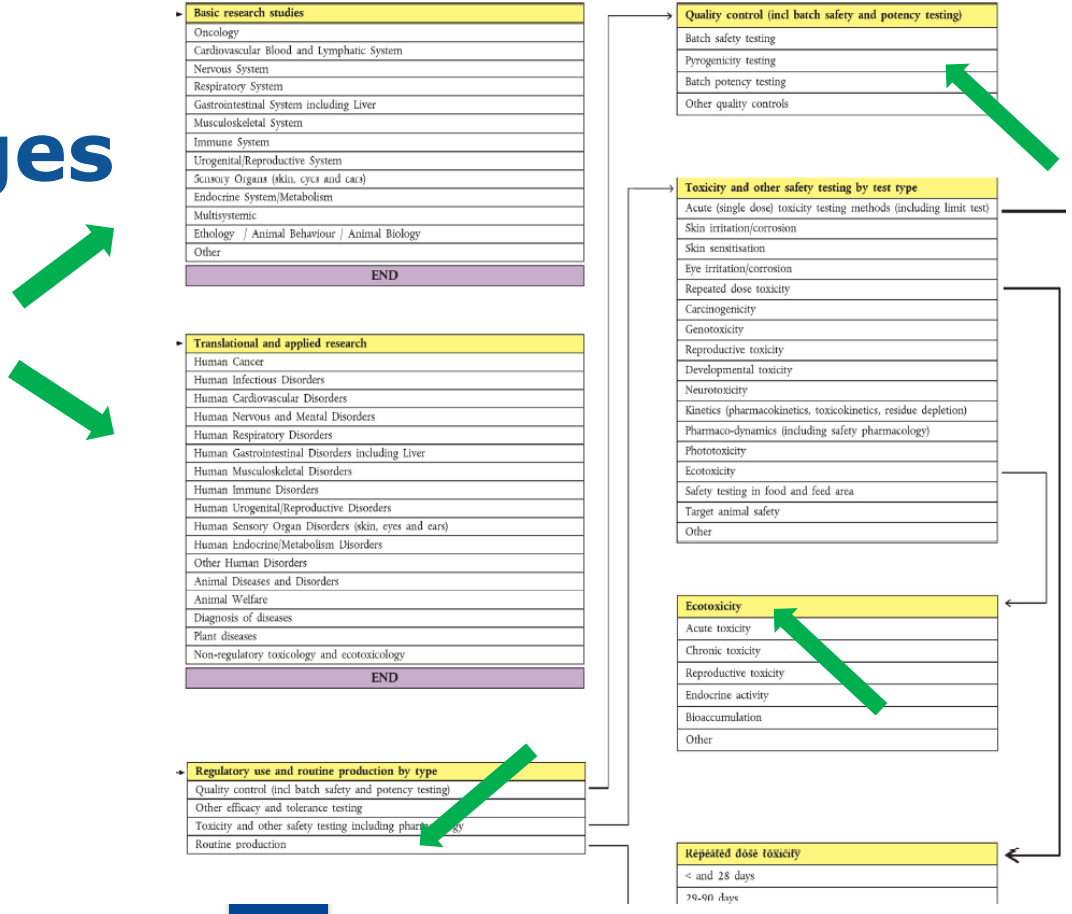

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2013 - 2019

Two key events

- *Article 58 Review of the Directive (2017)*
- *Fitness Check on environmental reporting (2019)*

Experience - User community reflections on NTS

- *"My job is to do science, not communication"*
- *How to explain technical, scientific work in a simple, concise manner?*
- *How to ensure accurate presentation of harms?*
- *How to articulate realistic benefits?*

Experience – drawing from Directive Review

Issues by

- users (authors)
- competent authorities reviewing NTS
- audience

Issues by audience with

- timeliness
- accuracy of content
- accessibility and
- searchability

Recommendations: Transparency

Recommendations

- Training for scientists (EU Education and Training Framework Module 11) should include training on requirements and expectations of non-technical project summaries.
- Member States should ensure that non-technical project summaries are published in a timely manner.
- Competent authorities, through the project evaluation and authorisation processes, should ensure that non-technical project summaries are accurate, fairly represent harms and be realistic about the expected benefits to improve the quality of non-technical project summaries.
- The Commission services, Member States and stakeholders should explore possibilities of a central repository of (or provide easy, searchable access to) all non-technical project summaries at EU level taking into account the legal requirements and linguistic limitations.

Opportunity to amend the Directive via environmental reporting Fitness Check

- *Modern tools & centralised data storage to improve*
  - **efficiency**
  - **availability and access (one-stop shop)**
  - **usefulness (search facility)**
  - **timeliness and relevance of data**
- *Improve uptake of the Three Rs*
- *Strengthen evidence base for future polices*

Outcome

Regulation (EU) 2019/1010 adopted 5 June 2019 amending Directive 2010/63/EU to have:

- *Publication and access to **non-technical project summaries***
- *Publication and access to **statistical data** on use of animals for scientific purposes*
- *Publication of reports on implementation*

Article 43 on non-technical project summaries

- *From 1 January 2021, **publication of NTS** within **six months** of authorisation*
- *Commission to establish a **central**, **open access, searchable database** for NTS*

Article 54(2) on statistics

- *MS to submit annual statistical data to the Commission electronically*
- *Commission to establish a **central**, **open access, searchable database** for statistics*
- *Commission to provide annual EU summary*

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- *2013 - 2019*
- *Transparency in the service of reduction of animal numbers and Refinement*

European Commission

REPLACEMENT /REDUCTION

Areas consuming ***most animals***

REFINEMENT

Purposes resulting in ***most severe uses***

EU database on NTS

- *Better understanding of specific areas of animal use*
- *Opportunity to gain insight in the areas of highest use volumes and severities*
- *Three Rs efforts already in use in these areas &*
- *New Three Rs opportunities through RA results*

Moving transparency to the next level

- *First EU report on statistics – expected soon*
- *Revised Commission Implementing Decision 2012/707/EU*
- *Technical preparation with MS during 2020*
- *NTS database operational by June 2021*

Thank you for your attention!

More information at:

http://ec.europa.eu/animals-in-science