



Directive 2010/63/EU

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

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*
- *Demonstration 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**



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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 leukaemia	
Duration of Project	Five years	
Key Words (maximum of 5)	Tumour; leukaemia; chemotherapy; radiation; mouse	
Purpose of Project (as in Article 3)	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
Describe the Objectives of the Project (e.g. the scientific unknowns or scientific or clinical needs being addressed)	Maintenance of colonies of genetically altered animals, not used in other procedures	No
	Leukaemia is a cancer of the bone marrow. Treatment of adults with leukaemia is unsatisfactory with only a minority being cured. Drugs against acute myeloid leukaemia were discovered in the 1950s, but no more effective drugs have been discovered since then. For a common type of adult leukaemia, acute myeloid leukaemia, most patients die from the disease despite chemotherapy. New approaches to developing drugs are required. A problem with leukaemia is that it appears to go away completely, but relapses after treatment has ended. This may be because a few 'tough' leukaemia cells (leukaemic stem cells) survive and grow again. We will study how leukaemia 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 leukaemic 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 leukaemic 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 leukaemia 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 anticipated 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. Leukaemia will then be induced by intravenous injection of leukaemic bone marrow. Mice with leukaemia 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 leukaemia 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 leukaemias take weeks to months to develop, we used other ways to study leukaemia 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 leukaemia cells into the mice. This allows us to study how the leukaemia grow over several weeks.	
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.		
2. Reduction		
Explain how the use of minimum numbers can be assured	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 treatment 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.	
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 (harm) 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 treatment 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.	

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



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2. Key changes

Other Amphibians (other than <i>Xenopus</i>)	
Zebra fish (<i>Danio rerio</i>)	
Other Fish (other than <i>Danio rerio</i>)	
Cephalopods (Cephalopoda)	
Re-use	
Re-use	
YES	Non-human primate?
	NO
Non-human primate - source	Place of birth
Animals born at a registered breeder within EU	Animals born in the EU at a registered breeder
Animals born in rest of Europe	Animals born in the EU but not at a registered breeder
Animals born in Asia	Animals born in rest of Europe
Animals born in America	Animals born in rest of world
Animals born in Africa	
Animals born elsewhere	
Non-human primate - generation	
F0	
F1	
F2 or greater	
Self-sustaining colony	
Genetic status	
Not genetically altered	
Genetically altered without a harmful phenotype	
Genetically altered with a harmful phenotype	
Creation of a new genetically altered line	
Animals used for the creation of a new genetically altered line/strain	
Severity	
Non-recovery	
Mild (up to and including)	
Moderate	
Severe	
Purposes	
Basic research	END
Translational and applied research	END
Regulatory use and routine production	END
Protection of the natural environment in the interests of the health or welfare of human beings or animals	END
Preservation of species	END
Higher education or training for the acquisition, maintenance or improvement of vocational skills	END
Forensic enquiries	END
Maintenance of colonies of established genetically altered animals, not used in other procedures	END



2. Key changes

Basic research studies
Oncology
Cardiovascular Blood and Lymphatic System
Nervous System
Respiratory System
Gastrointestinal System including Liver
Musculoskeletal System
Immune System
Urogenital/Reproductive System
Sensory Organs (skin, eyes and ears)
Endocrine System/Metabolism
Multisystemic
Ethology / Animal Behaviour / Animal Biology
Other
END

Translational and applied research
Human Cancer
Human Infectious Disorders
Human Cardiovascular Disorders
Human Nervous and Mental Disorders
Human Respiratory Disorders
Human Gastrointestinal Disorders including Liver
Human Musculoskeletal Disorders
Human Immune Disorders
Human Urogenital/Reproductive Disorders
Human Sensory Organ Disorders (skin, eyes and ears)
Human Endocrine/Metabolism Disorders
Other Human Disorders
Animal Diseases and Disorders
Animal Welfare
Diagnosis of diseases
Plant diseases
Non-regulatory toxicology and ecotoxicology
END

Regulatory use and routine production by type
Quality control (incl batch safety and potency testing)
Other efficacy and tolerance testing
Toxicity and other safety testing including pharmacology
Routine production

Quality control (incl batch safety and potency testing)
Batch safety testing
Pyrogenicity testing
Batch potency testing
Other quality controls

Toxicity and other safety testing by test type
Acute (single dose) toxicity testing methods (including limit test)
Skin irritation/corrosion
Skin sensitisation
Eye irritation/corrosion
Repeated dose toxicity
Carcinogenicity
Genotoxicity
Reproductive toxicity
Developmental toxicity
Neurotoxicity
Kinetics (pharmacokinetics, toxicokinetics, residue depletion)
Pharmacodynamics (including safety pharmacology)
Phototoxicity
Ecotoxicity
Safety testing in food and feed area
Target animal safety
Other

Ecotoxicity
Acute toxicity
Chronic toxicity
Reproductive toxicity
Endocrine activity
Bioaccumulation
Other

Repeated dose toxicity
< and 28 days
28-90 days

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*

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 policies*

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*

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 of animal numbers and Refinement*

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](http://ec.europa.eu/animals-in-science)

