



Guidance Document on Genetically Altered Animals (GAA)




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Part 1. Administrative Procedures



- Legal Framework information
- Activities falling under the definition of a procedure and requiring a project authorisation
- Flow chart for the requirements for a project authorisation for the creation and maintenance of GA lines
- Type of projects and authorisation processes

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GAA's under the Directive



- Developed together by all key stakeholders
- Published in all EU languages

https://ec.europa.eu/environment/chemicals/lab_animals/pubs_guidance_en.htm



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Clarification of terms "GAA"



- Extract from 2020/569/EU; Annex III, Part B, Section A General Provisions; paragraph 11.1

"genetically altered animals" include

- genetically modified (transgenic, knock-out and other forms of genetic alteration) and
- naturally occurring or induced mutant animals as per the definition in Article 3(1).

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Guidance on GAAs under the Directive



Part 1: Administrative procedures
➢ a table on activities requiring a project authorisation

Part 2: Three Rs in the creation, breeding and maintenance of GAA


Part 3: Welfare assessment schemes

Part 4: Transferring welfare information on GAA


Part 5: Reporting of genetically altered animals
➢ Annual statistical reporting
➢ 5-year implementation report

Appendices I-IV
➢ Appendix II: Project application and evaluation including illustrative examples

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Clarification of terms "Creation"




Development of a new line of GAA

- deliberate/intentional gene alteration e.g., genetic insertion/deletion/editing chemical mutagenesis or other manipulation of a gamete or embryo
- Cross-breeding of two pre-existing lines
- Maintenance of spontaneous mutants

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Tissue sampling and genetic characterisation (1)




- Genetic characterisation with methods below minimum threshold is not covered by the definition of a "procedure"
- Tissue obtained from the identification of the animal is not covered by the definition of a "procedure"

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Maintenance of an existing non-harmful phenotype line




Lines which have a Welfare Assessment (as described in Part 3) demonstrates **no harms** above the minimum threshold of pain suffering, distress or lasting harm is likely to occur **during a lifetime of the animal**
e.g., some green fluorescent protein (GFP) lines

Lifetime – this should mean the natural life of the animal

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Tissue sampling and genetic characterisation (2)



- Tissue sampling using invasive methods for the sole purpose of genetic characterisation is considered a "procedure" **requiring a project authorisation and subsequent statistical reporting**
- Tail biopsy in mice and fin clipping in fish are not generally considered methods of identification/markings – thus such methods **require project authorisation**

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Part 2. 3Rs in creation, breeding and maintenance of GAA




- GA specific examples and suggestions

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Maintenance of an existing GA line



Project authorisation required

Breeding of an **existing harmful phenotype line**

Welfare Assessment (as described in Part 3) demonstrates

- risk for a harmful phenotype above the minimum threshold of pain, suffering, distress or lasting harm during the lifetime of the animal.

Includes refinement in breeding protocols
e.g., heterozygote x wild-type

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Part 3. Welfare assessment scheme for most common GAA



- General considerations
- Section A. Welfare assessment template for all species and time points
- Section B. Welfare assessment template for specific species (rodents; fish; farm and mini-pigs; chickens)

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Part. 5 Reporting of GAA



- General legal framework
- Flow chart for the requirements for statistical and implementation reporting for the creation, maintenance and use of GAA
- Annual statistical reporting
- Implementation report every five years

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Annual statistical reporting – GAA related activities and actual severity



Actual severity should reflect the highest severity of all techniques performed on the animal including

- Adverse effects from the genetic alteration
- Invasive tissue sampling
- Vasectomy / Superovulation / Embryo transfer, etc.

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GAA creation - Annual statistical reporting



- **Report all animals used for creation in the annual statistics**
with the exception of:
- **Genetically normal offspring (wild type) is not reported in annual statistics provided the animal has not been tissue sampled using an invasive method**

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5-year Implementation Report



Animals bred, killed and not used (5th year)

- **Report all remaining animals not reported in the annual statistics**

Creation: genetically normal offspring (wild type)

Maintenance:

- Non-harmful lines: animals killed on the 5th year and not tissue sampled using an invasive method
- Harmful lines: animals killed on the 5th year, not having expressed harmful phenotype, neither tissue sampled using an invasive method

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GAA maintenance – Annual statistical reporting



Maintenance of harmful phenotype line

- Some animals are **used** – report as other uses
- Under maintenance - **Only report animals that have expressed the harmful phenotype and killed without being used in a procedure**
and

Maintenance of non-harmful phenotype line

- **Report animals when animals were killed and tissue sampled using an invasive method (=requires project authorisation)**

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Annexes




- Annex I: Examples of database of GA lines
- **Annex II: Project application and evaluation for the creation and maintenance of GA lines**
- Annex III: Bibliography
- Annex IV: Glossary of terms

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Annex II



- Introduction
- Part A. Illustrative examples of key information required in **GAA project application**
- Part B. Illustrative examples of the **evaluation** of GAA project proposals

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Part B. Example of the evaluation of GAA project proposals




- It is targeted at **project evaluators**
- This part is of interest also to project applicants: it allows a better understanding of the considerations to be given during the evaluation process to ensure Directive obligations are met

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Part A. Examples of key information required in GAA project application



The elements described in Annex VI of the Directive are not necessarily in an order which can be easily followed when building a project application

A table maps the order of the elements in Annex VI to the order in which the elements are further developed within Part A

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Summary



Guidance provides more clarity on the legal obligations for GA animals complemented with illustrative examples

Thank you for your attention!
We hope you find the document helpful

https://ec.europa.eu/environment/chemicals/lab_animals/pubs_guidance_en.htm



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Background



- GA lines are generally created and used to contribute to:
 - **scientific knowledge (basic science) or**
 - **for applied science e.g. to develop therapies for disease**
- However, some projects use specialised teams to produce GA lines for use in science by others
- Considerations vary
 - **Science**
 - **Service**

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