Directive 2010/63/EU

Making progress together implementing the Directive

Strasbourg, France
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EP Intergroup "Welfare and Conservation of Animals"
Making progress together

• Directive: objectives and the Three Rs
• Implementation process
  ▪ National legislation
  ▪ Operational structures
  ▪ Guidance and dissemination of good practice
• Current work
Objectives

- **Increased animal welfare** through a systematic implementation of the Three Rs

- **Improved science** through new approaches, improved models, better statistical design
  - from reduced stress to reduced ‘noise’ and variability

- More **efficient use of resources** and focus on essential through minimum red tape
Objectives

• *Intensify the work on alternatives* - also for improved predictivity, faster output, creation of new business opportunities

• *Increase public confidence* through improved transparency and enforcement, improved information provision
Article 1

“Subject matter and scope”

1. This Directive establishes measures for the protection of animals used for scientific or educational purposes. To that end, it lays down rules on the following:

(a) the replacement and reduction of the use of animals in procedures and the refinement of the breeding, accommodation, care and use of animals in procedures; ...”
REPLACEMENT

REDUCTION

REFINEMENT
Three Rs

- **Three Rs central** in project planning, evaluation/authorisation, during and after

- Three Rs to be applied in **all interaction** with animals, *also when not in a project* e.g. breeding, accommodation and care

- New tools for the development, validation and uptake of **alternative approaches** to progress towards the **ultimate goal of full replacement**
The implementation process

- National legislation
- Operational structures
- Common understanding and guidance
- Experience – illustrative examples and good practice
- Revisit and expand where needed
Legal framework

- *Directive 2010/63/EU entered into force in 2010*
- *Adoption of national legislation by 10 Nov 2012*
- *Directive fully applicable from 1 Jan 2013*
Correct, complete and timely transposition is key

- Level playing field, reliable operational environment and increased animal welfare
- All 28 Member States notified transposition
- The Commission examines the completeness as well as the correctness of all national legislative measures
The implementation process

1. National legislation
2. Operational structures
3. Common understanding and guidance
4. Experience – illustrative examples and good practice
5. Revisit and expand where needed
Project leaders, animal technologists, animal care takers

Animal Welfare Body

Designated veterinarian

CAs for project evaluation and RA

Inspectors

National Committee and National Contact Point

Named persons for animal welfare, information, competence

Legislation, codes of practice, guidance

Efficient COMMUNICATION network
Implementation challenges

- Coherent **understanding**
- Available resources - administrations and operators
- Existing infrastructures and practices
- Help and guidance on new elements
New Directive: New Culture

- Change of mindset: Three Rs and transparency
- From imposed to self-motivated application - rolling out the concept of culture of care
- Buy-in and commitment by all affected
The implementation process

- National legislation
- Operational structures
- Common understanding and guidance
- Experience – illustrative examples and good practice
- Revisit and expand where needed

Facilitate overcoming the challenges
Coherent implementation

European Commission works with Member States and stakeholder organisations to promote a coherent implementation through

- Member States' meetings
- Expert Working Groups on Key Topics
- Information portal on Commission website
The Expert Working Groups

- Reach common **understanding** of the issues
- Agree on a **common framework** and **approach**
- Agree on **criteria** and **principles**
- Recommend **good practice** and **optimum processes**
- Provide practical, demonstrative examples to facilitate understanding
Guidance endorsed by all Member States

- *EU Education and Training Framework*
- *Project Evaluation and Retrospective Assessment*
- *Severity Assessment Framework*
- *Animal Welfare Bodies and National Committees*
- *Inspections and Enforcement*
- *Three Rs Information Flow*
Animals used for scientific purposes

Introduction

The protection and welfare of animals is an area covered by a wide range of EU legislation. This includes the protection of wildlife, zoo animals, farm animals, animals in transport and animals used for scientific purposes. Animal studies, whether for the development or production of new medicines, for physiological studies, for studying environmental effects or for the testing of chemicals or new food additives, has to be carried out in compliance with EU legislation.

Since 1986, the EU has had in place specific legislation covering the use of animals for scientific purposes. On 22 September 2010 the EU adopted Directive 2010/63/EU which updates and replaces the 1986 Directive 86/609/EEC on the protection of animals used for scientific purposes. The aim of the new Directive is to strengthen legislation, and improve the welfare of those animals still needed to be used, as well as to firmly anchor the principle of the Three Rs, to Replace, Reduce and Refine the use of animals, in EU legislation. Directive 2010/63/EU took full effect on 1 January 2013.

Latest updates

- NEW New events added to our events page
- NEW Link provided to the Expert Group on the Application of the 3Rs in Regulatory Testing of Medicinal Products (JEG 3Rs) of EMA on the Links page
- NEW New search tool for alternatives added to our Three Rs pages
- NEW All 28 Member States have adopted their respective national legislation to transpose Directive 2010/63/EU. Congratulations!
- NEW The next report has been uploaded to the Member State activities to advance the "Three Rs" and an update made to National Contact Points
- The Commission and the industry partners have committed to the continuation of the European Partnership for Alternative Approaches to Animal Testing (EPAA) for 2016-2020
Current work

- *Illustrative examples of project evaluation process* (Jun 2015)

- *Statistical data collection EU*

- *Three Rs reporting*
  - [http://ec.europa.eu/environment/chemicals/lab_animals/3r/advance_en.htm](http://ec.europa.eu/environment/chemicals/lab_animals/3r/advance_en.htm)

- *Kick-off meeting National Committees* (Dec 2015)

- *Preparatory work for review (starting in 2016)*
The work continues – let’s keep the momentum going!

Counting on you!
Thank you for your attention!

More information at:

http://ec.europa.eu/animals-in-science
Implementation of Directive 2010/63/EU: - the animal welfare perspective

Kirsty Reid
Scientific Officer Research Animals | Eurogroup for Animals
@KirstyEG4A
There will be no improvement to animal welfare without proper implementation.
• Animal use remains one of concern for EU citizens
• The Directive 2010/63/EU will only be effective if implemented to its fullest
• Much more needs to be done on 3Rs
• Biomedical research needs to be considered more closely
Implementation and enforcement

- Harmonisation across the member states
  - Use of guidance, building on the guidance developed
  - Sharing best practices

- Working together can only make things stronger
  - Cooperation between all players is essential

- Proper enforcement
  - Inspections
  - Auditing
  - Where in breach of the directive – infringement procedures/closures

We all have responsibilities!!!
Stakeholder engagement
The only way to **guarantee good animal welfare** is to ensure that EU member states put in place the necessary **mechanisms to implement, control and monitor effectively**...

- Deadline for transposition was 2012 - Final transposed in **March 2015**!
- **Conformity checks** by the Commission – checking systematically both the completeness and the correctness of all member states transposition of Directive
• Germany - **animal welfare examples of poor transposition**:  
  - objectives for an impartial and independent assessment by the competent authority have not been transposed correctly in the German Animal Welfare Act  
  - **Translation**: Art 38 “justified” was changed to “if presented to be scientifically proven”, ("gerechtfertigt" vs. “wissenschaftlich begründet”)  
  - **Different requirement to Directive**: procedures involving animals for purposes of education, training, and advanced vocational training with methods that have already been established **do not need** to be authorized (in principle, an authorization is foreseen to be mandatory for all scientific procedures involving animals  
  - Etc

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*Ruhdel et al, Comment in Altex 31, 2/14*
• Developed in expert working groups involving Com, MS and stakeholder experts.
• Endorsed by National Contact Points
• Available in all languages soon
• The Guidance needs to be taken up in MS in all establishments
• Not legally binding, not restricted to minimal measures rule therefore key players need to work together to make them more robust and promote their use.

http://ec.europa.eu/environment/chemicals/lab_animals/interpretation_en.htm
This is the first time EU legislation spells out the principle of the 3Rs of replacement, reduction and refinement and makes it a firm legal requirement!!!!
Replacement in Directive

• Recital 10: ‘…However, this Directive represents an important step towards achieving the final goal of full replacement of procedures on live animals for scientific and educational purposes as soon as it is scientifically possible to do so…’

• Recital 49: ‘…Such review should examine the possible replacement of the use of animals, and in particular non-human primates, as a matter of priority where it is possible, taking into account the advancement of science…’

Eurogroup question to Commission, member states, scientists –
What is being done at EU and national levels in relation to replacement of animal use?
Why? - To fully comply with the requirements of the directive in relation to the 3Rs is not easy due to a lack of information, guidance or expertise at the level of individual establishments and their animal welfare bodies, or even at a national level.

Eurogroup supports and recommends that member states consider establishing a national centre to act as appoint of reference to assist in fulfilling the requirements to:-

- Carry out project evaluation (Art 38)
- Contribute to the development and validation of 3Rs (Art 47)
- Dissemination of information on the 3Rs by the member states (Art 47)
- Proper functioning and composition of animal welfare bodies (Art 26, 27)
- Establishing National Committees (Art 49)
Examples in Member States:

- NC3Rs and FRAME (UK), FICAM (FI), IPAM (IT), SWETOX (SE), ZEBET (DE), RIVM (NL)
- Animal welfare organisation, Dyrenes Beskyttelse are a partner and co-fund with the pharmaceutical industry the Danish 3R-centre (from 1 Jan 2014) and will be involved (at least) for a 3 year period.
  [http://www.foedevarestyrelsen.dk/english/Animal/Pages/The-Danish-3R-Center.aspx](http://www.foedevarestyrelsen.dk/english/Animal/Pages/The-Danish-3R-Center.aspx)
- Romanian Centre for Alternative Methods (ROCAM) will be formally established on the 5th June 2015. It intends to become a central point of expertise on 3Rs in Romania
- CAAT-Europe
- Non EU: NORECOPA (Norway)
Establishing, promoting and maintaining a good ‘culture of care’ is a fundamental requirement if legal, ethical and animal welfare obligations, along with wider responsibilities towards employees and the public, are to be met.

Evidence that the ‘right’ culture is in place:
Good and focused Management, Communication, and 3Rs and animal welfare

Ultimately, to achieve high standards of animal welfare and science, a wide range of factors have to come together to provide the right framework within an organisation.

- Having the right attitudes, values and people, with everyone engaged and positively contributing, knowing what is required of them and doing the right thing without prompting!
Authorisation is an integral and crucial part of the Directive, with all projects, personnel and establishments needing some form of authorisation BEFORE animal use.

- Competent Authorities (CA) (Art 59) are designated by the MS and are key to implementation and enforcement
  
  **Eurogroup calls for the CA’s to:**
  - Have sufficient trained staff and resources to carry out their duties.
  - To facilitate the spread of good practice
  - Enforce compliance

- Project evaluation (Art 36 – 38) critical aspect and is carried out by CA.
  
  **Points of interest to Eurogroup:**
  - In many instances experiments are badly designed, carried out or reported, this wastes animals' lives and causes suffering that could have been avoided.
  - How challenging will project evaluators be when carrying out harm-benefit assessment or when reviewing whether all opportunities for implementing 3Rs have been taken?
  - A number of MSs appear to have delegated the project evaluation task to a local establishment level - how can we ensure impartiality or avoid conflicts of interest!?

- Authorisation of breeders, suppliers and users (Chapter IV) is the responsibility of the member state.
  
  **Eurogroup calls for Member States:**
  - Only establishments in full compliance be granted authorisation, and are inspected regularly.
Non-technical summaries

Required under the Directive for projects classified as severe and those using non-human primates, but can be waived for projects containing procedures that are non-recovery, mild, or moderate, and not using non-human primates, that are necessary to satisfy regulatory and some production or diagnosis purposes (Article 43)

- Template developed - not a legal requirement
- Situation in MS: Many setting up system, DE has developed a data-base, UK required NTS for all projects, DK has 30 years experience …
- There is a need to share best practices
- Problems:
  - They indicate more benefits than stating expected harms
  - Concerns that some countries may publish under other countries

Transparency is mainly covered in Article 54 on ‘Reporting’. By 10 November 2018 and every 5 years thereafter, Member States must send the Commission information on implementation of the Directive – including Non technical summaries
Good non-technical project summaries are a vital aid to public understanding and accountability regarding animal use, and make a significant contribution to transparency. They should include the potential harms and benefits, how the 3Rs are considered and how the regulations are being applied in practice. Therefore meaningful and relevant information should be made available in the summaries.

**Eurogroup position:**
- To request NTS for *all* projects
- To ensure harmonisation across all member states
- to ensure that the information provided is an honest account of the harms to animals and benefits involved
Severity assessment

Classifying the severity of procedures (Art 15, annex VIII) and setting an upper limit is a critically important component of the Directive. Levels of suffering are classified as mild, moderate or severe.

Eurogroup’s focus:

• Any level of suffering is a concern to us, but **ending severe suffering must be a top priority.**
• Working with the scientific community is very important if we are to produce innovative, challenging and feasible approaches to reducing and ultimately ending severe suffering.

Concern of Eurogroup:

• How well are people undertaking the task of reporting the actual severity experienced by each animal - or are they just guessing, generalising or putting what the prospective classification was??
• Is the severity assessment framework guidance that has been developed being taken up and used (includes tailor made scoring sheets, observation tools, agreement on terminology)
Inspections by the Member States (Art 34): MS shall ensure that Competent Authorities carry out regular inspections of all breeders, suppliers and users.

- The Commission, member states and stakeholders have developed guidance on Inspections and Enforcement.

Eurogroup’s concern:
- Some MSs only plan to carry out only the very minimum number of inspections of establishments - and wording of the Directive means the same third of establishments can be inspected every year. There is no maximum interval between one being visited.

Controls of Member State inspections (Art 35): The Commission shall, where there is due reason for concern, undertake controls of the infrastructure and operation of national inspections.
The standards (Art 33 and Annex III) are adapted from Appendix A of Council Convention ETS 123.

**Eurogroup request to establishments:**
- We call for higher welfare to be considered as these set out the minimum standards and requirements
- Develop national guidelines*
- To implement the Annex III without delay (regarding spacing)

* Incorporating explanatory text from ETS123 or use Felasa Euroguide
Binding Annex III

- Combines “Performance” and “Engineering” Standards
- Promotes social housing
- Promotes environmental complexity and enrichment
Annex III  RODENTS
Minimum enclosure sizes (cm²)

<table>
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<tr>
<th></th>
<th>Current</th>
<th>New Annex III (1/1/17)</th>
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<tbody>
<tr>
<td>Mice</td>
<td>180</td>
<td>330</td>
</tr>
<tr>
<td>Rat</td>
<td></td>
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</tr>
<tr>
<td>250g</td>
<td>350</td>
<td>800</td>
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<tr>
<td>over 600g</td>
<td>350</td>
<td>1500</td>
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<tr>
<td>Guinea Pig</td>
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<td>600g</td>
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<td>2500</td>
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<tr>
<td>Gerbil</td>
<td>NS</td>
<td>1200</td>
</tr>
</tbody>
</table>
Care and accommodation of animals

Rodents

Social housing
Secure areas
Materials to encourage natural behaviour, e.g. gnawing
Comparisons of new requirements for Minimum Enclosure Areas: 4kg Macaque

- **USA**
- **Can**
- **UK**
- **Old EU**
- **New EU**

- **Min. Enclosure size (m²)**
- **Min. Height (m)**

* * 2 animals
** * 4 animals
A retrospective assessment of some projects shall be carried out by the competent authority. This considers whether the objectives were achieved, the harms to animals and 3Rs issues (Article 39).

Eurogroup believes there are animal welfare, scientific and project management benefits to retrospective review.

Eurogroup request:

• Retrospective assessment should be extended to **include a review and critique of the species and study design**. This approach would help to avoid repetition of animal studies that did not yield useful results. Without a retrospective assessment and review of the limitations of the model, it is possible that another group may try the same or similar studies.

• We urge that retrospective assessment takes place for **all** projects.
The current implementation of Directive 2010/63

Magda Chlebus, Director Science Policy
EP Intergroup for Animal Welfare
21 May 2015
The lifecycle of a research project

Example: Find a more efficient treatment for Parkinson disease
First step: Identify a new biological target
Method: Study of cognitive function in animal models (rodents)

Many steps before a study can be done – and after…
Directive 2010/63 applies at every step

- Scientific justification
- Application of 3Rs
- Choice of species
- Severity
- Reuse

- Application
- Ethical review/benefits and risks
- Authorisation by competent authorities
- Non technical summary

- Sourcing of animals
- Authorized establishment
- Trained personnel
- Identification
- Inspections

- Animal Welfare Bodies
- Named veterinarian
- Housing and Care
- Anesthesia
- Reuse

- Reporting numbers and severity
- Euthanasia
- Retrospective review
- Sharing tissues
- Setting free/rehoming

D I R E C T I V E  2 0 1 0 / 6 3  –  D I R E C T I V E  2 0 1 0 / 6 3
Implementation of Directive 2010/63

- The experience is still relatively limited & not all countries advance at the same pace

- The responsibility for adequate implementation is a shared one:
  - The scientific & welfare community must support training, dissemination of information/guidance, good practice sharing
  - EU monitoring implementation and impact, advice/guidance, exchange good practice
  - Human & financial resources

- Impact of some national provisions should be monitored, e.g.
  - Training in anaesthesia possible only during original vocational training
  - E-learning not allowed even for limited theoretical courses

- Scope will impact on numbers
Evolving research paradigm

- It is happening – questions, tools and regulations are evolving driven by scientific progress and collaboration

- More shall be done
  - National and European research projects to further alternatives and scientific paradigm shift
  - Effective validation and processes for regulatory acceptance in Europe and globally
Examples of IMI outputs that support **new research paradigms**

- Identification and validation of new drug targets and novel hit and lead discovery
- Establishment of robust, validated tools for preclinical drug development
- Development of biomarkers and tools predictive of clinical outcomes (efficacy and safety)
- Clinical trials - improved design and process
- ‘Big data’ solutions to leverage knowledge
- Implementation of data standards
Collaborative projects deliver 3Rs – examples

- Eliminating poorly predictive models
  - Parkinson’s Disease
  - Diabetes
  - Asthma
  - Chronic Pain
  - Schizophrenia
  - Depression
  - Autism

- Developing new improved models
  - Parkinson’s Disease
  - Diabetes
  - Asthma
  - Chronic Pain
  - Schizophrenia
  - Depression
  - Autism

- Replacing animals with better in vitro & in silico models
  - Diabetes
  - Cancer
  - Schizophrenia
  - Chronic pain
  - Drug safety
  - Parkinson’s Disease

- Alternative tools
  - Biomarkers
  - Novel cell lines
  - 2D and 3D cell cultures
  - Imaging
  - Computation
  - Simulation
  - Pooling & novel analysis of existing data
Update on Ongoing IMI Projects

The Innovative Medicines Initiative (IMI) is Europe’s largest public-private initiative aiming to speed up the development of better and safer medicines for patients. The IMI supports 30 projects with a combined budget of over €600 million covering drug safety & efficacy, knowledge management, and education.

Pharma IQ in conjunction with The Predictive Toxicology Summit 2013, provide an update on the 9 ongoing IMI projects concerning drug safety.

MARCAR, A NEW WAY OF TRACKING TUMOR DEVELOPMENT
Start date: 01/01/2010
Duration: 60 months
Contributions Total Cost: €13,319,233

MIP-DILI, PREDICTING DRUG-INDUCED LIVER-INJURY
Start date: 01/02/2012
Duration: 60 months
Contributions Total Cost: €32,400,000

SAFESCIMET, DELIVERING BETTER TRAINED SCIENTISTS FOR PHARMACEUTICAL R&D
Start Date: 01/01/2010
Duration: 60 months
Contributions Total Cost: €6,653,588

ETOX, PREDICTING SIDE-EFFECTS OF DRUGS EARLY IN DEVELOPMENT
September 2012 the ETOX library is opened
Start date: 01/01/2010
Duration: 60 months
Contributions Total Cost: €1,865,461

SAFE-T, DETECTING DRUG SIDE EFFECTS AT AN EARLIER STAGE
Start date: 15/06/2009
Duration: 60 months
Contributions Total Cost: €35,871,055

PROTECT, STRENGTHENING THE MONITORING OF THE SAFETY OF MEDICINES
Start date: 01/09/2009
Duration: 60 months
Contributions Total Cost: €29,810,615

ABIRISK, MAKING NOVEL DRUGS SAFER FOR PATIENTS
Start Date: 01/03/2012
Duration: 60 months
Contributions Total Cost: €34,900,000
Recent examples:
http://bit.ly/1HnCRN6
Points to consider

- Full and correct implementation is key

- It is a joint responsibility: scientists, authorities, animal welfare

- Scientific progress:
  - Scientific innovation drives 3Rs
  - partnerships, EU and national funding, regulatory acceptance