Human Relevant Models in Biomedical Research

Progressing Science through Innovative Approaches

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The European Union Reference Laboratory for Alternatives to Animal Testing

EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing

Established under Directive 2010/63/EU on the protection of animals used for scientific purposes

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ANNEX VII

DUTIES AND TASKS OF THE UNION REFERENCE LABORATORY

1. The Union Reference Laboratory referred to in Article 48 is the Commission's Joint Research Centre.
2. The Union Reference Laboratory shall be responsible, in particular, for:
   - (a) coordinating and promoting the development and use of alternatives to procedures including in the areas of basic and applied research and regulatory testing;
   - (b) coordinating the validation of alternative approaches at Union level;
   - (c) acting as a focal point for the exchange of information on the development of alternative approaches;
   - (d) setting up, maintaining and managing public databases and information systems on alternative approaches and their state of development;
   - (e) promoting dialogue between legislators, regulators, and all relevant stakeholders, in particular, industry, biomedical scientists, consumer organisations and animal-welfare groups, with a view to the development, validation, regulatory acceptance, international recognition, and application of alternative approaches.
3. The Union Reference Laboratory shall participate in the validation of alternative approaches.

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Why use alternative models in biomedicine?

ETHICS and SCIENCE

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THE GREATEST NUMBER OF ANIMALS IS USED IN RESEARCH

Statistics on the use of animals for scientific purposes in the Member States of the European Union and Norway in 2019

→ 72% animals used in basic and translational/applied research
→ about 50% (5 million) used in biomedical research

- Moderate-Severe procedures: 42%
- Non-recovery: 6%

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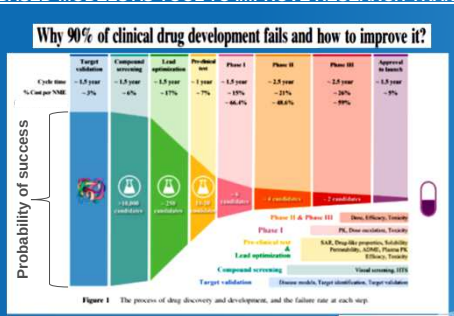
HUMAN-BASED MODELS AS TOOL TO IMPROVE RESEARCH TRANSLATION



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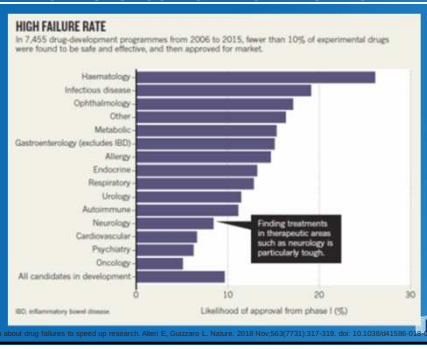
HUMAN-BASED MODELS AS TOOL TO IMPROVE RESEARCH TRANSLATIONAL



Be open about drug failures to speed up research. Allen E. Gozzaro L. Nature. 2018 Nov;563(7731):317-319. doi: 10.1038/d41586-018-07477-7.

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Biomedical reviews areas

- Incidence/prevalence of human diseases
- Number of animals used and severity of procedures

- 322,827 abstracts screened
- 89,446 full texts analysed
- 3049 non-animal methods selected

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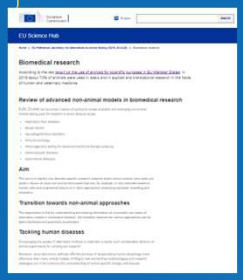
HOW TO FIND THEM & WHAT THEY LOOK LIKE



- Technical Report
- Executive Summary
- Leaflet
- JRC Data catalogue

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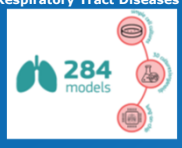
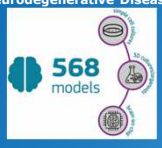
GENERAL FINDINGS

- Preferred methods differ among research areas
- Those involving cells are the most common (except for one area)
- Steady increase in the use of Organ-on-Chip in certain areas

Respiratory Tract Diseases



Neurodegenerative Diseases



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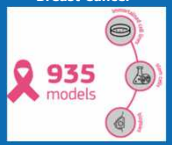
GENERAL FINDINGS

Breast Cancer



Immuno-oncology

Cardiovascular diseases

Immunogenicity testing for ATMP

Autoimmune diseases

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Database example (respiratory tract diseases)

Model no.	Disease Area	Disease Feature	Category	Type	Application	Biological Endpoints	Throughput	Potential
1	Lung Cancer	Epithelial Mesenchymal Transition (EMT)	3D Spheroid Co-culture	A549 cell line	Disease mechanism (exp/theor)	Gene expression	Medium / Low (Lab scale)	Mechanistic Stud
1	Lung Cancer	Epithelial Mesenchymal Transition (EMT)	3D Spheroid Co-culture	Mesenchymal Stem Cells (MSCs)	Disease mechanism (exp/theor)	Gene expression	Medium / Low (Lab scale)	Mechanistic Stud
2	Lung Cancer	Angiogenesis	3D Spheroid Co-culture	A549 cell line	Disease mechanism (exp/theor)	Vascularisation	Medium / Low (Lab scale)	Mechanistic Stud
2	Lung Cancer	Angiogenesis	3D Spheroid Co-culture	murine 344SQ	Disease mechanism (exp/theor)	Vascularisation	Medium / Low (Lab scale)	Mechanistic Stud
2	Lung Cancer	Angiogenesis	3D Spheroid Co-culture	murine 393P	Disease mechanism (exp/theor)	Vascularisation	Medium / Low (Lab scale)	Mechanistic Stud
3	Lung Cancer	EGF/EGFR expression	2D or 3D Culture	A549 cell line	Drug development/testing	Gene expression	Medium / Low (Lab scale)	Drug Discovery
4	Lung Cancer	Tissue/Cell Viability	Chip or microfluidic system	A549 cell line	Drug development/testing	Tissue / Cell Viability	Medium / Low (Lab scale)	Drug Discovery
5	Pulmonary Disease	Angiogenesis	2D or 3D co-culture	Human Pericytes	Model development -	Vascularisation	Medium / Low (Lab scale)	Mechanistic Stud
6	Lung Cancer	Inflammatory no specific feature	3D or 3D co-culture	Murine Lung microenvironment	Model development -	Imaging	Medium / Low (Lab scale)	Diseases Progres
7	Lung Cancer	Toxicity	Spheroid	HepRG (liver cells)	Inhalation toxicity	Metabolism	Medium / Low (Lab scale)	Toxic insult/repair
7	Lung Cancer	Toxicity	2D or 3D co-culture	Primary human NHBE cells	Inhalation toxicity	Metabolism	Medium / Low (Lab scale)	Toxic insult/repair
8	Lung Cancer	Structural Changes	2D or 3D Culture	A549 cell line	Drug development/testing	Morphology	Medium / Low (Lab	Diseases Progres

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Target Audience

- Research groups submitting a project proposal which makes use of living animals;
- Animal Welfare Bodies advising research groups on project proposals;
- Competent Authorities responsible for project evaluation;
- National Committees coordinating the project evaluation process, dissemination of information and sharing of best practice within each Member State;
- National Contact Points responsible for the implementation of the Directive in the Member States

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EXAMPLE OF USE

Irish organisation

HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Scientific Animal Protection
Regulatory Update – November 2022

7 EURL ECVAM UPDATE: NON-ANIMAL MODELS

We are pleased to inform you that a sixth database on non-animal models has been published by The European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM). This new database contains detailed descriptions of 449 non-animal models being used for research into **cardiovascular diseases**. An accompanying Technical report and Executive summary have also been published. We would like to remind all researchers working in any of the **six scientific areas** for which EURL ECVAM non-animal model resources exist, that it is imperative to consult the relevant resource in order to search for potential non-animal alternatives, prior to designing an animal study. Applications for such studies submitted to the HPRA without evidence of the relevant database search will be returned to the applicant.

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Work in progress

- The EP funded a Pilot Project to develop an automated database to collect and structure alternative methods for use in biomed research.
- Machine learning algorithms or AI will be trained on the available datasets
- We aim to complete the project by 2024, when a consolidated version of the dataset should be published.

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Thank you!

EURL ECVAM

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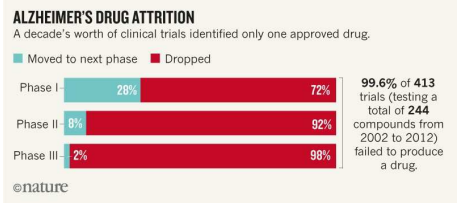

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