Annual meeting as a 2 day symposium –
This year with several European speakers

More than 140 participants. Please use the opportunity for networking. Presentations are covered and with abstracts and selected PDFs of presentations.
Program 10th November

News from 3R centres and activities

DK: European engagement, survey, teaching, 3R prize, grants

NC3R: More than 10 years 20 employed, supported 238 major awards, active interaction with researchers, SMEs, industry Acute tox study with impact on ICH M3 guideline, Data sharing, Arrive, Crack it, ExpDesignerAssistant. Discussion about inclusion of animal welfare organisations
Program 10th November

**News from 3R centres and activities**

Århus: Symposium on Metaanalysis 16+17. November

Novo Nordic: 4 persons engaged in new 3R unit focusing on internal projects and internal collaborations. First in the world. Established on ethical grounds.
Program 10th November

**News from 3R centres and activities**

Presentation of last years 3R projects supported by the 3R centre:

Polyclonal antibodies in chicken – Otto Kalliokoski

In vitro human skin model – Mette Elena Skindersøe

In vitro model to predict lung toxicity – Søren Thor Larsen
‘Home’Teaching material for high school from 3R centre

Undervisningsmateriale om forsøgsdyr og de 3R’er

Undervisningsmateriale er tilskyndet de gymnasiale uddannelser i fagene Biologi A og Bioteknologi A.

Undervisningsforløb

Vigtigt: Læs lærervejledningen og følg derefter undervisningsmaterialets 5 trin:

1. Quiz - første del (send dit navn til ranon@fvsr.dk og modtag login til quiz indenfor to arbejdsdage)
2. Forsøgsdyr og 3R (film)
3. 3R - vejen mod færre og mere skånsomme dyreforsøg (baggrundstekst)
4. Gruppearbejde med udgangspunkt i ressource-rummet.
5. Quiz - anden del

(Undervisningsmaterialet bliver i nærmeste fremtid suppleret med yderlige to artikler)
‘Resource room’ – group assignments (detailed and deeper understanding)
The 3Rs: on animal scientists’ perceptions, awareness and practices

Overall aim: to improve the basis for further implementation of the 3Rs in Denmark and establish a baseline for assessing future implementation

Research questions
1. What is the level of awareness and knowledge about the 3Rs among Danish animal scientists?
2. To what extent are the 3Rs implemented in practice?
3. What are the barriers for further implementation?
Summing-up the obstacles and opportunities

• Viewed as a whole, most welcome the 3Rs and see no obstacles
• The publicly employed see more obstacles than the privately employed
  • Obstacles are mainly technical/innovational

• Increased data sharing is seen as an important means to achieve an overall reduction of the number of animals used

• Replacement generally not considered as feasible as the other Rs and seems to be the greatest challenge
  • progress could be achieved by education
Preliminary findings

Number of animals used

- Offentlig 38% (1.2%)
- Privat 62% (6.1%)
- I alt 100% (4%)
Preliminary findings

Types of investigations – selected years

- Biological investigations
- Medical, odontological and veterinary medical investigations
- Quality control medical, odontologic
- Quality control veterinary
- Toxocological safety assessments
- Diagnostic
- Uddannelse og undervisning (T2_8)
- Andet (T2_9)

Percentage comparison between 2002 and 2005.

Fig. 1: Numbers of animals used for scientific purposes in 16 core European countries
Data obtained from European Commission reports on the statistics on the number of animals used for experimental and other scientific purposes in Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxemburg, Portugal, Spain, Sweden, Switzerland, The Netherlands and United Kingdom for the years 1996, 1999, 2002, 2005, 2008 and 2011; corresponding data from Switzerland were obtained from the Swiss federal food safety and veterinary office; (A) Total number of animals used (green circles), and detail numbers for research and development for medicine, veterinary and dentistry, summarized as medical research (red triangles), biological research, which refers to basic biological research (blue squares) and medical + biological research combined (purple diamonds). (B) The proportion of animals used for the purpose of safety assurance, i.e., toxicological testing (red triangles), for diagnostic (blue squares) and education purposes (green circles).

Fig. 3: Proportion of genetically modified animals of the total number of animals
The graph shows the annual percentage of transgenic animals of the total animals used for scientific purposes from 2002 to 2012 in the United Kingdom (UK, red triangles), Germany (DE, blue squares) and Switzerland (CH, green circles). Data are calculated from annual publications on statistics on animals used for scientific purposes from the German Federal Ministry of Food and Agriculture (BMEL), the UK Home Office and the Swiss Federal Food Safety and Veterinary Office (BLV).
Posters presented

Al-Malahmeh et al, Wagening University: Physiologically based kinetic modelling of bioactivation of myristirum facilitating risk assessment

Yishi Huang et al, Dansih Nanosafe Centre: The constrained drop surfactometer as a toll for toxicological assessment of impregnation spray products

Alayjlouni AM et al, Wagening: Mode of action based risk assessment of the botanical food-borne alkenylbenzene apiol from parsley using physiologically based kinetic (PBK) modelling and read across to safrole
Animals used for scientific purposes

Search Tools

- **EURL ECVAM Search Guide (the Guide)** – The Guide is particularly helpful to inexperienced database users. It represents a useful resource where comprehensive searches for alternatives are required as part of authorisation processes for animal experiments and where regulatory requirements mandate the application of the Three Rs. The Guide provides examples of search procedures and user guidance to facilitate the location of the desired information on Three Rs alternatives; it also includes an inventory of relevant resources, contains a check list (the seven golden steps) to allow for searches in a structured and systematic manner, moreover, search principles, suggested search terms etc. Free copies of the handbook or a pdf version are available from the EU Bookshop.

- **Go3R** is a free of charge ‘semantic’ search engine making use of underlying expert knowledge on 3Rs methods to semantically retrieve Three Rs-relevant information. Currently, the semantic Go3R tool searches in the databases PubMed and TOXNET. Additionally, Go3R allows searching the entire World Wide Web using a Google search with automatic higher ranking of 3Rs relevant websites. Results of PubMed and TOXNET searches are presented to the user together with a dynamic table of contents highlighting 3Rs information and allowing to quickly restrict vast search results to relevant documents. The Go3R expert knowledge covers the entire scientific domain of alternatives to animal testing in all biomedical disciplines, but has a special focus on regulatory toxicity testing.

- **Search.norecopa.no** is a search engine for Norecopa’s four databases: 3R Guide, NORINA, TextBase and Classic AVs. The search engine takes into consideration the words which have been entered by the user; an index of all the words in the databases; a list of synonyms constructed specifically for these databases; an “auto-complete” function which suggests search terms based on the search engine’s own dictionary; algorithms which prioritise or suppress words depending on their relevance; Boolean operators, which the user can edit and “fuzzy logic” (words resembling those entered by the user). The user can limit the search to one or more of Norecopa’s four databases, or to one or more of a variety of search fields and scientific disciplines.
However..

“Simply meeting the legislate requirements will not ensure appropriate welfare, care and use practices”

Requires commitment

Commitment enabled through institutional support

Institutional support facilitated via regulatory support
Culture of **Challenge**

*Challenge – the path for discovery*

**Researcher**

- Right questions?
- Right disciplines?
- Right models?
- Beyond obvious?

- Refinement..
Conclusions

Legal framework, partners and networks in place to strive strategically for new alternative approaches – take part

From aspiration to practical, continued implementation of the Three Rs

Three Rs is everyone’s responsibility

Time to roll out Culture of Challenge
  - for the benefit of science and animals
Definition of QSAR:
Quantitative Structure-Activity Relationship

A QSAR is a mathematical model (often a statistical correlation) relating one or more parameters derived from chemical structure to a property or activity, e.g. a toxicological endpoint

See e.g. EU chemicals legislation, REACH, guidance R.6: "QSARs and grouping of chemicals" for more information
New Danish QSAR predictions database

A new online Danish QSAR predictions database expanded to 60,000 substances and applying battery predictions forms a number of software systems, with a completely new interface and engine, will be published in November 2013 at the site http://qsarodb.dk.

Search sections and basic clauses
- Combined clauses
- Defining a clause
- Adding a clause
- Executing a clause

Search results
- Saving / loading query trace

Search examples
- CAS search
- Name search
- Database affiliation search
- Parameter search

Fragment search
- Fragment editor
- Cyclic and acyclic structures
- Specific wildcards (Atom lists)
- wildcard atoms

More search examples
- Aromatic example
- Quaternary nitrogen example
- Aldehyde example
- Wildcard atom example
- Specific wildcard atom (atom list) example

Your comments and questions are welcome. For more information, please contact LMC.
Stem cells as tools to address the 3Rs

- Stem cells
  - Simple in vitro assays
    - Microfludic systems
  - Organoids/3D models
    - Organs-on-chip
  - Whole organ models

Animal models

Complexity
CAAT 2.1 – a vision and a strategy
led by Thomas Hartung
Hannes remarks

Awareness internally and externally of lab animals welfare through education, communication and dialogie

Review of a lot of applications for permits and of protocols of animal experimentation

Stop for the use of many thousands of mice, rats, rabbits for batch control of efficacy and purity of insulins glucagons, growth hormone and FVII

Stop for use of thousands of mice for production of monoclonal antibodies by the ascites method

Introduction and use of better anestesia and analgesia

Improvement of housing and environmental enrichment

My 1 priority as lab animal vet has been to be available for the animals, the animal technicians and the scientists
Announcement of Workshops 14-18 August 2016 at Panum, University of Copenhagen with 3R

Bridging genomics, human environmental health risk assessment and the 3Rs in animal science

to be organized by the Nordic Environmental Mutagen Societies (NordEMS) and adhered to program of the European Environmental Mutagen Societies (EEMS), and European Concensus Platform of Alternatives (ECOPA) in August 2016 in Copenhagen.

Organising committee: Lisbeth E. Knudsen, University of Copenhagen, Denmark (chair)
Jørn A. Holme, Norwegian Institute of Public Health, Head of Norwegian Society of Pharmacology and Toxicology (NSFT)
Margareta Törnqvist, Stockholm University, Sweden
Tuula Heinonen, president of FICAM and SSCT, Finland
Kristín Ólafsdóttir, University of Iceland