Need for further research on alternative tiered testing strategies

Animal experiments in numbers

EU 2011:

11,5 m. vertebrates

Germany 2015:

Ca. 2,8 m. vertebrates (+ decapods)

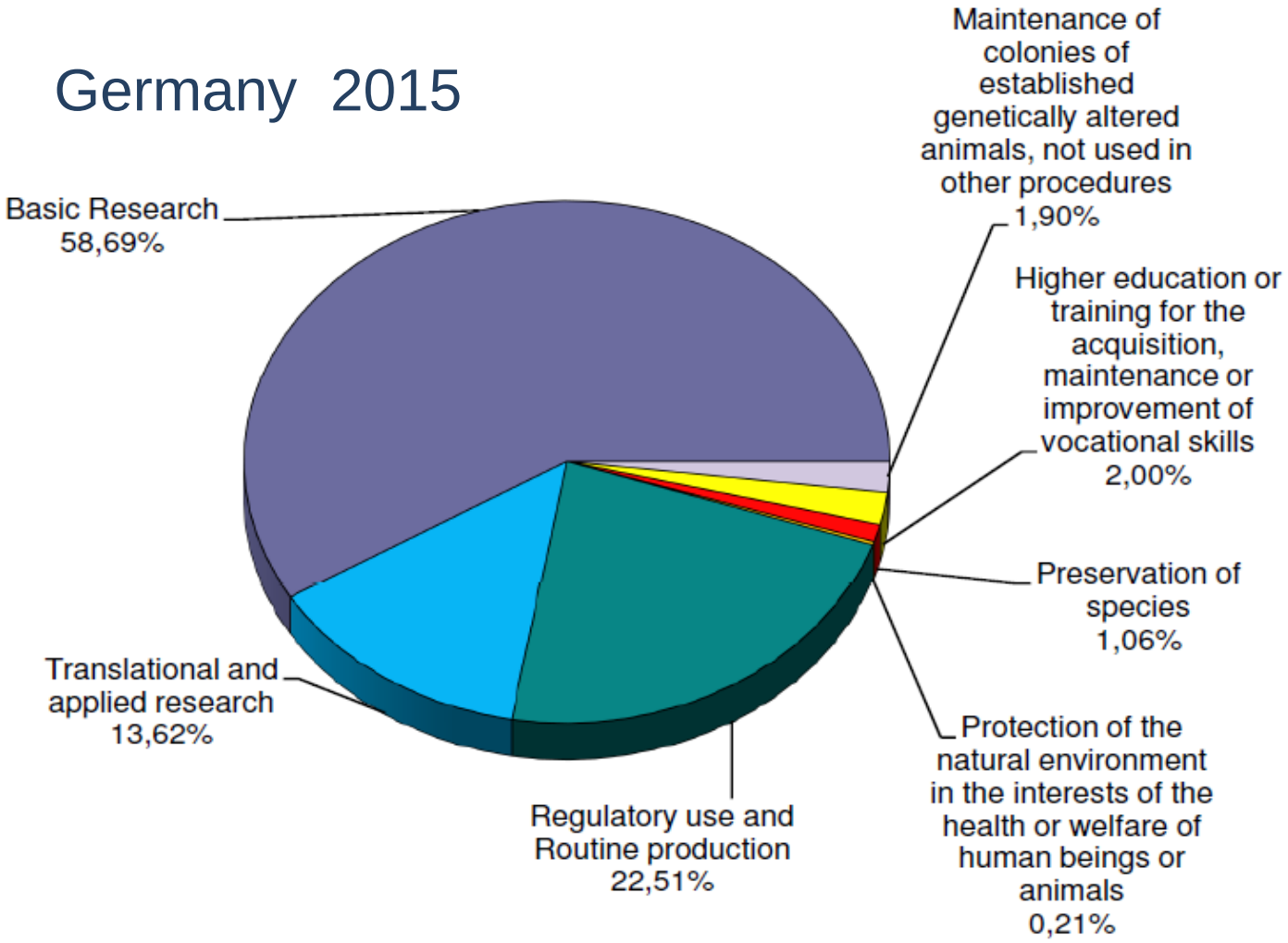
Animals that were used for regulatory purposes:

630.255 vertebrates (+decapods)

Animals required for testing of one PPP substance:

Up to 12.000 vertebrates

What purposes are animals used for?



What does animal testing/an experiment mean for the animal?

Many purposes of animal use, but for all is true:

Animals experience pain, distress, fear and harm

…..and death awaits many of them at the end of the tests/experiments or they are used in other procedures

Disregarding the actual experiment the following impairments need to be considered

- origin
- transport
- breeding and housing
- handling

→ considerable constraints in species-appropriate behaviour

→ psychic strains: fear, stress, behavioural disorders etc.

Position of the German Animal Welfare Federation

Ethical and scientific arguments speak against animal use

- Responsibility for animals instead of „survival of the fittest“
- High capacity for suffering, pain perception

- Lack of transferability
- Benefit questionable
- Modern alternative methods available or have to be developed

Risk assessment: protection of consumers, animals and the environment vs. animal welfare?

Common goal:

Protect humans, animals and the environment from risks

→ New substances are supposed to be safe

→ Close data gaps

→ Substitute dangerous substances with low-risk substances

Risk assessment: current approach

- Animal experiments are still the gold standard even though a variety of validated and more modern alternative methods exist

→ Currently, risk assessment always initiates animal testing

- Animal testing in toxicology includes some of the cruellest tests known
  - Animals are poisoned though they are fully conscious

    →Poisoning results in e. g. cramps, internal bleeding, organ failure, respiratory paralysis, death
  - Pregnant females and pups are involved
  - Unrealistically high dosing of test substances
  - In „repeated dose studies“ suffering for the animals accumulates

(Stress because of handling, repeated administration of high dosages, substance effects)

Risk assessment: myth

„Animal testing is indispensable for protection of consumers and of the environment“

BUT

- most test methods relying on animals are outdated (established in the 1940s)
- have never been properly validated to demonstrate their relevance to humans
- studies are published continuously that proof:

→ results from animal tests are not reliable, hard to reproduce and difficult to translate to humans

- superiority of intelligent testing strategies

Animal free test methods in risk assessment

Tiered testing strategies: combination of all available test methods

Step-wise assessment of a substance in single tests

- Results of a test

  weight of evidence → information sufficient?

  is follow-up testing in the next tier necessary?
- Starts with the evaluation of all existing information:

  tests that were already performed

  available data from humans
- Analysis of physico-chemical properties
- *in silico* tests
- *in vitro* tests
- (*in vivo* tests only as a last resort)

Replacement or at least Reduction of animal testing

Example Testing strategy

Skin sensitisation

Up to now: test on guinea pigs or mice (LLNA)

New: animal free test battery:

(a) What happens on chem. level on skin surface?
(b) How do skin cells react?
(c) Is the immune system activated?

→ Stepwise insight into allergic potential of a substance

What can we learn from other legislation/areas of risk assessment?

- Enshrine in legislation that animal testing should only be used as a last resort (REACH)
- Replace outdated animal tests with adopted animal free tests/testing strategies (BPD)
- Waiving of data requirement (REACH)
- Read-across from other substances (REACH)
- Harmonize data requirements from all areas of risk assessment ; use the most progressive approach
- Use data from risk assessment of substances for different legislations

Is the use of the new EFSA Guidance for the risk assessment of metabolites going to lead to more animal testing?

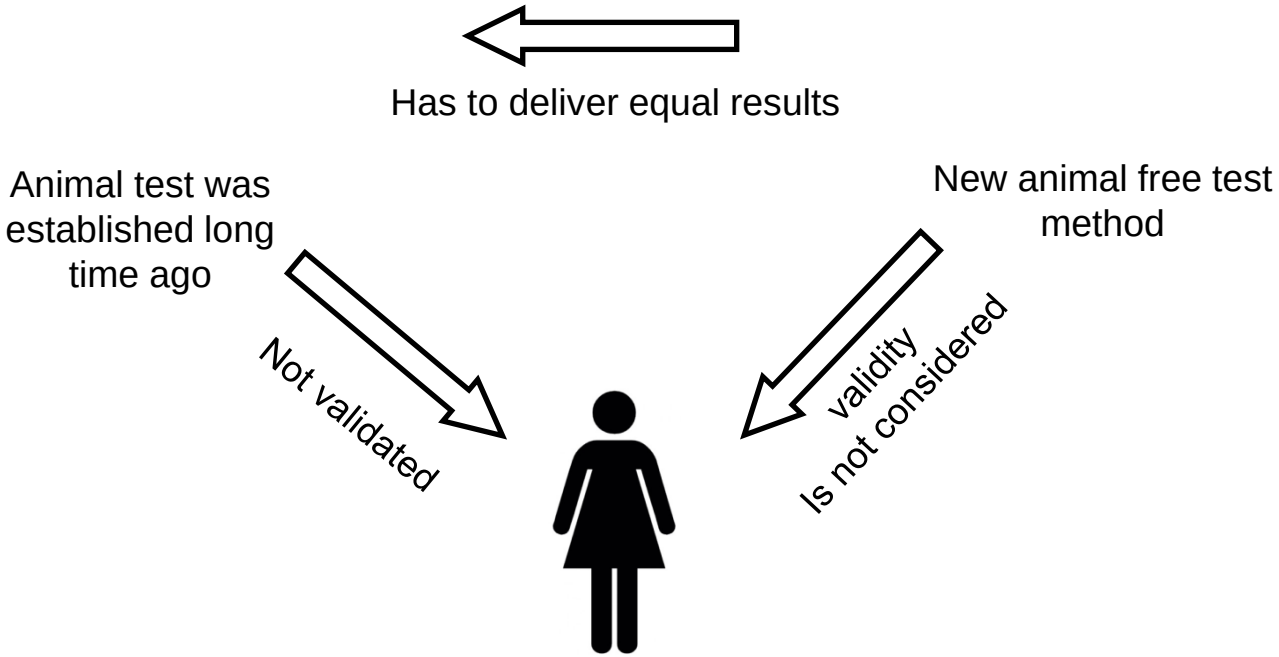
yes!

- Many triggers for „further actions“ by risk assessors/managers (even though decisions should be made case by case)
- *in vivo* follow up testing in test battery for assessment of genotoxicity
- Assessment of general toxicity:
  - enhanced 28-day study (OECD TG 407)
  - 90-day rat study (OECD TG 409)
  - reproduction/developmental toxicity screening test (OECD TG 422)
  - developmental toxicity study (OECD TG 414, 416 and 443)
  - ad hoc toxicity studies or additional toxicity studies

→ testing strategy is a step in the right direction
→however, still too much focus on *in viv*o testing

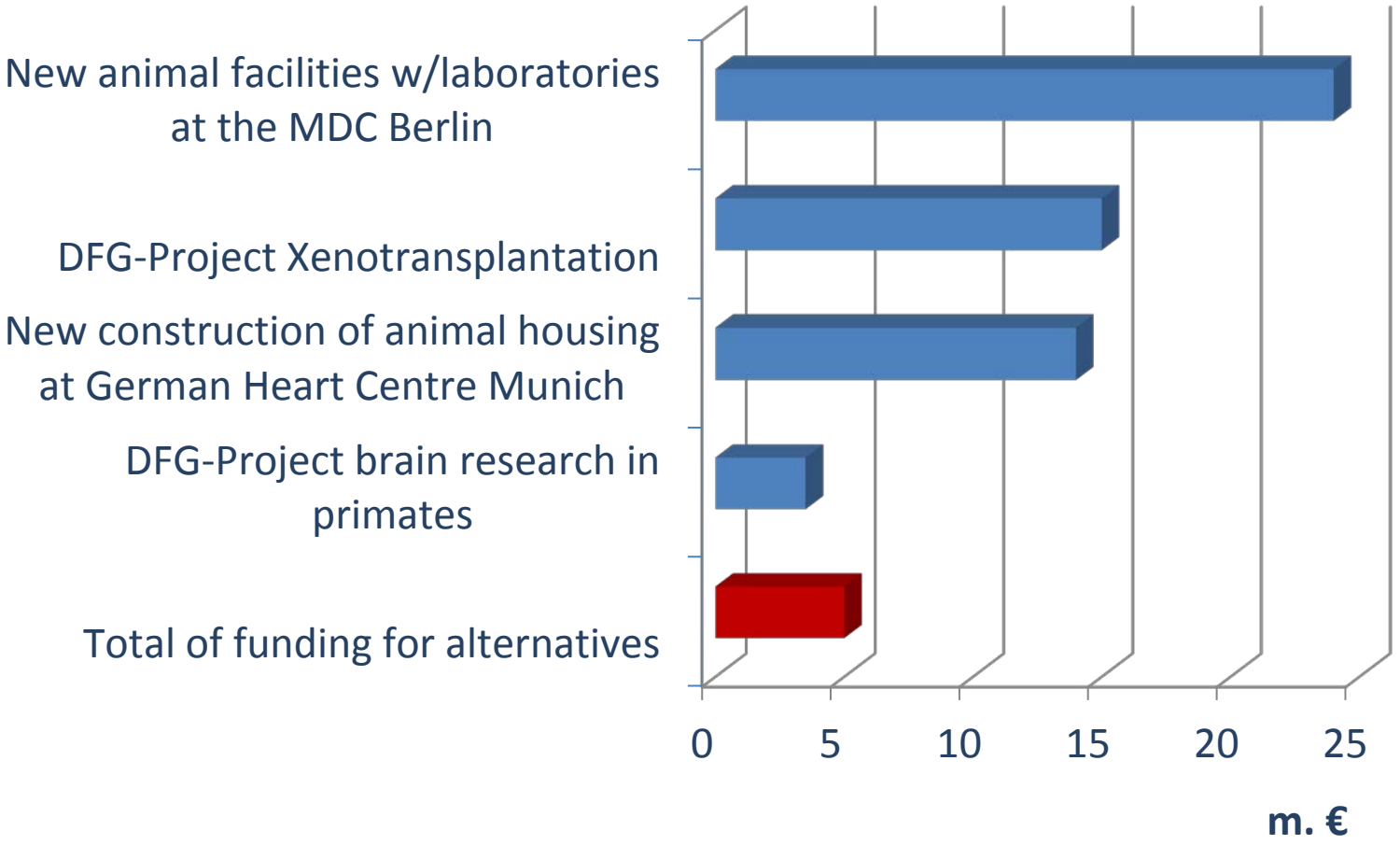
Challenges

Most of the time unrealistically high demands for alternative test methods



Challenges

No shortness of ideas – but of funding!



Our demands

Full replacement of animal testing/experimentation – animal-free testing strategies for risk assessment

Politics:

- Adaption of legislation and data requirements to encourage animal-free test methods and testing strategies
- Development of a strategy with measures to replace animal use for science, testing and education with clearly set goals
- Increase of funding for development of animal free methods and testing strategies for research, testing and education;

Authorities:

- ethical evaluation, also for regulatory testing (needs to be clarified by legislative organ)
- stricter evaluation and also rejection of applications
- support and strengthen use of alternative methods

Science and industry :

- push for use of alternative methods
- invest in development of animal free test methods and testing strategies

Thank you for your attention!

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