

Provision of Environmental Enrichment— Scientifically Proven or Use of Common Sense?

Introduction

To this day, the use of animals in research is essential for all pharmaceutical companies in the processes of discovery, development and production of new pharmaceutical products. Companies are required to provide appropriate data regarding efficacy, safety and toxicology from testing in both animals and people before the authorities will approve a new product. So, while we recognise that we cannot eliminate the use of animals completely, we are committed to doing everything we can to minimise the number of animals used and to ensure that the animals we do use are treated well.

The new EU Directive 2010/63/EU, which must be transposed into the member states national law effective January 1, 2013, sets out minimum standards for housing and care, including requirements for incorporation of enrichment initiatives¹.

Annex III of the Directive sets out requirements for animal housing and husbandry and the environment of the animals; their behavioural needs and enrichment are explicitly mentioned. It will depend

The new EU Directive 2010/63/EU, which must be transposed into the member states national law effective January 1, 2013, sets out minimum standards for housing and care, including requirements for incorporation of enrichment initiatives¹.

largely on the people responsible for the animals at the user, supplier and breeding establishments how effectively this is implemented and it is our joint responsibility to read the Directive with an open mind and a will to apply the spirit, as well as the letter, of the law².

In the beginning of year 2000, Novo Nordisk, in a unique partnership with the Danish Animal Welfare Society,

established new standards for housing animals, with the aim of improving animal welfare and minimising stress. The housing conditions of mice, rats, guinea pigs, rabbits and dogs were initially reviewed based on the needs of the animals, disregarding the existing housing systems, and financial and technical considerations. The identified basic needs of the animals were then prioritised, resulting in a description of how these needs ideally could be met in captivity; subsequently, new housing systems were developed and introduced³.

Enriched housing conditions for rats does not impact scientific outcomes

A number of studies have expressed concerns that environmental enrichment may increase uncontrollable variation in the animals, thereby creating the need for greater numbers of animals. Within neurobiology, there may be a scientific basis for such concern⁴. However, even though there could be a negative impact within neurobiological research,

continued on page 6

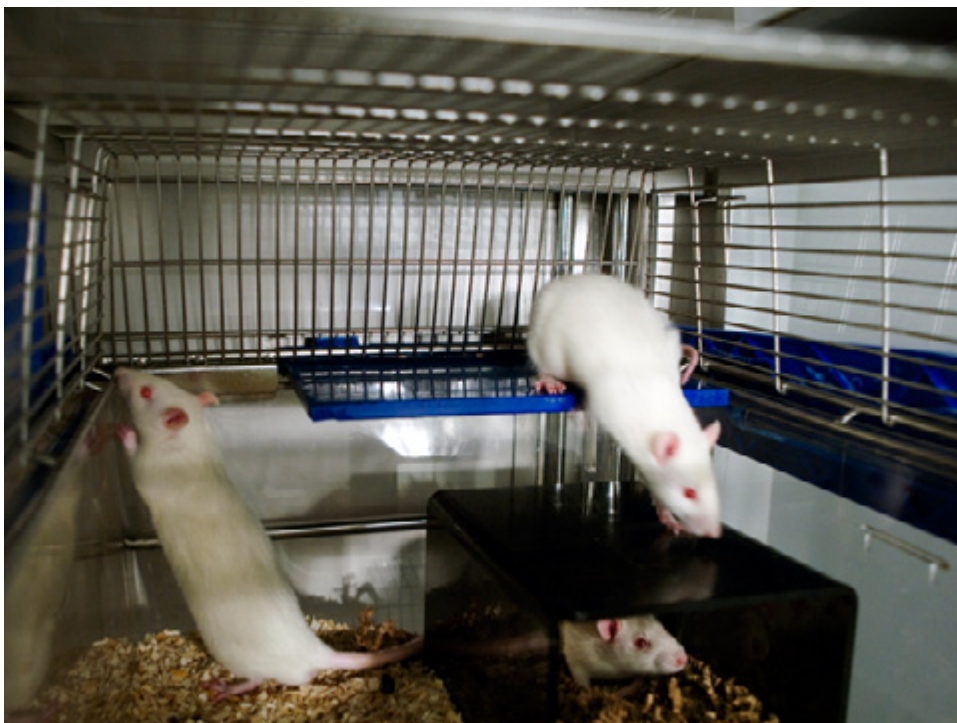


Figure 1: Novo Nordisk RAT CAGE

Type IV cage measures 1800 cm²/279 in² and is 32 cm/12.6 inch high. There is a built-in shelf (400 cm² / 62 in²) and the floor is covered with aspen bedding. The cage contains paper-based nesting material, a gnawing stick and a hide. Finally, corn and maize are provided twice a week to encourage foraging behaviour. The number of rats per cage depends on the weight of the rats (e.g. max. 5 rats weighing up to 400 grams).

there is not necessarily any basis for concern within other research areas.

In the new housing systems we developed for rats (Fig. 1), we demonstrated in preference tests that the rats actually prefer to stay in an enriched environment compared to an un-enriched cage⁵. We then initiated studies to explore whether clinical pathology and cardiovascular parameters were influenced by housing rats under environmentally enriched conditions. Male Sprague-Dawley rats were housed under three different regimes:

non-enriched, standard-enriched (according to Annex III of the Directive) and the extra-enriched Novo Nordisk cages. A total of 41 different parameters were monitored via daily observations, clinical pathology, telemetry and coagulation tests and virtually no differences were observed in relation to the manner in which the rats were housed⁶. Furthermore, six traditional behavioural tests were done to evaluate the impact of enrichment on group-housed animals. The basic activity level of the animals was assessed using the open-field test.

This test was combined with an amphetamine challenge test. The level of anxiety was evaluated by use of the elevated plus maze test. Secondly, a Morris water maze study was done to assess spatial learning abilities. Thirdly, two more complex learning ability tests were performed, namely the water Y-maze and the conditioned avoidance task. The different housing conditions did not influence the level of activity, the level of anxiety or the response to amphetamine. Neither did the differences in housing conditions influence the learning abilities of the animals in the Morris water maze or the Y-maze. However, in the conditioned avoidance task, rats housed in the extra-enriched environment demonstrated significantly fewer avoidances than rats housed under non-enriched conditions⁷.

Clearly, it is impossible to conclude that there will never be any variation in relation to these differences in housing conditions, but in terms of clinical pathology, haematological or cardiovascular pathology, there is no basis, thus far, for denying rats environmental enrichment due to fear of a changed parameter expression or increased uncontrollable variation.

Figure 2. Novo Nordisk DOG PEN

Pens each consisting of an indoor area of 2-3.8 m²/ 21.5-40.9 ft² (and connected through a hatch to an outdoor pen of approximately 2m²/21.5 ft²). The individual pens can be connected in a flexible way, allowing dogs to be standard group housed, but still fed individually. All mature dogs are typically housed in harmonious groups consisting of 2-4 animals each.

All the indoor pens are enriched with platforms and ramps, which provide a choice of resting place and observation opportunities, offering the dogs visibility across the room. The dogs are given various other types of toys for playing and biting, as well.



Figure 3. Novo Nordisk DOG OUTDOOR ENCLOSURES

The outdoor grass enclosure includes: a) pig huts with flat roofs that provide resting and observation opportunities: b) huge banks with underground tunnels: c) small stone formations used for observation: and d) trees and big logs for playing and marking.

Scientifically proven or use of common sense?

In an ideal world, of course, it would be nice to have the time and resources to prove everything scientifically and in many cases this is also the right approach. However, sometimes the use of common sense might be a better way to get things moving.

We decided to change the housing of our dogs:

- 1) From single housing to group housing in pens (Fig. 2),
- 2) To give all dogs daily access, in harmonious groups, to large outdoor enclosures for a minimum of one hour (Fig. 3),
- 3) To take the dogs for walks on a leash either alone or in small groups in the surrounding farmland,
- 4) To introduce a three-step, age-divided socialisation program to fulfil the need of early socialisation and on-going training, as well as to fulfil the need for close social interaction with humans.

It was common sense to us that by doing so we actually “provided an environment which takes into account the physiological and ethological needs of the species” as (later) stated in Annex III of the Directive and we saw no reason to scientifically prove this was good for the dogs and no signs that it interfered with the models we used the dogs for.

continued on page 8



Figure 4. Novo Nordisk RABBIT PEN

A pen system that measures 150x200 cm / 59x79 in (i.e. 30.000 cm² / 4.650 in²). The pens are fixed to the wall at waist height to minimise bending and lifting by animal care staff and to facilitate catching the rabbits. Plastic sheeting prevents the rabbits from escaping and reduces room allergen levels. Each pen is divided in two along its length by a partition that has pop holes to allow the rabbits to run through. Aspen bedding and a gnawing stick are provided and a shelter is placed on each side of the partition, so that rabbits can hide or hop on top. The rabbits have access to hay and are provided carrots, apples, etc. twice a week. The rabbits are housed in groups of 10 for short-term or eight for long-term projects.

Similarly, we saw no reason to scientifically prove that it was better for female rabbits to be group housed in large pen systems (Fig. 4) instead of single housed in the rather small cages we used to have. We use many rabbits for antibody production and we believed so much in the new housing system that we considered it a waste of time and money to setup scientific protocols to prove our idea was good.

It hadn't been scientifically proven in the beginning that

animals prefer to be in rather small barren cages. So why would we now have to scientifically prove that it is better to be in a large cage?

We believe improved housing with provision of environmental enrichment will cover the basic needs of the animals to a much higher degree than the traditional cage systems; therefore, we recommend that housing like this should be used for housing of experimental animals. Beyond ensuring much better welfare of the animals, the new systems are much

more pleasant and inviting, creating a much better working environment and contributing to a broader acceptance by the public of experimental animal use.

Acknowledgements

Especially, I would like to thank Lars Friis Mikkelsen for many fruitful discussions regarding the enriched rat cage studies. However, all collaborators are thanked for the excellent science and common sense they have invested in the studies described. But, most importantly, I would like to acknowledge all the animal caretakers and animal technicians for their daily commitment to ensuring good animal welfare.

References

1. European Commission (2010), Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. *Official Journal of the European Union* L276: 33-79.
2. Sørensen DB and Hansen AK (2012). Drivers for enrichment in Directive 2010/63/EU. *The Enrichment Record*. Summer 2012: 13-15.
3. Ottesen JL, Weber A, Gürtler H and Mikkelsen LF (2004). New Housing Conditions: Improving the welfare of experimental animals. *ATLA* 32, Supplement 1, 397-404.
4. Bayne K (2005). Potential for unintended consequences of environmental enrichment for laboratory animals and research results. *ILAR Journal* 46: 129-139
5. Krohn TC, Mikkelsen LF, Sørensen DB, Haagensen AMJ, Hansen AK and Ottesen JL (2011). The ability of SD-rats to distinguish between three different housing environments. *Scand. J. Lab. Anim. Sci.* 38: 21-27
6. Mikkelsen LF, Sørensen DB, Krohn T, Lauritzen B, Dragsted N, Hansen AK and Ottesen JL (2010). Clinical pathology and cardiovascular parameters are not influenced by housing rats under increased environmental complexity. *Animal Welfare* 19: 449-460.
7. Sørensen DB, Mikkelsen LF, Nielsen SG, Ersbøll AK & Krohn TC (2011). The influence of enriched environments on learning and memory abilities in group-housed SD rats. *Scand. J. Lab. Anim. Sci.* 38: 5-17.