

Environmental conditions constantly maintained: the XenopLus Housing System

One of the elements not always taken into due account in the development of an aquatic system is maintaining constant micro-environmental conditions. At Tecniplast we have created a system with just this purpose in mind.

The XenopLus rack features a tank in which the water flows out from the lower part partially removing faeces and food piling up at the bottom of the cage. The inner, smaller plastic pipe has holes in the upper part through which water is delivered to the exhaust system beneath the tank and also acts as an overflow in case of anomalous clogging of the holes in the outer pipe. The tank can be emptied while still on the rack: it is thus practical to sanitize and it cuts out any ergonomic inconvenience to the operator.



The rack is made entirely of AISI 304 or 316 stainless steel; each standard rack holds 9 tanks, but customized versions can be provided on request. Shelves at all levels guarantee easy access to any of the tanks (again, with great ergonomic advantages for the user). The rack is available in two versions, one with feet and one with castors,

both adjustable, and is provided with high precision stainless steel valves to regulate water flow to each tank. The water flow in any single row may be cut off by means of any one of the three ball valves.

Given that the most important element to consider in the housing of these species is maintaining constant environmental conditions: the system has been designed to achieve this purpose by maintaining uniform levels of PH, Temperature, Water Flow, Conductivity and Nitrogen Waste.

Nitrogen levels are checked by biological filtration. Our biological filter provides a very large surface for beneficial bacteria while at the same time removing toxic nitrogens (NH_3 , NH_4^+ , NO_2^-).



PH and Conductivity can be buffered by means of the dosing pumps. When needed, the system pumps salts and buffer substances from a saturated solution (there is thus no need for the operator to check the quantities to be added).

Temperature is controlled through a heating and cooling system, water flow through a pressure equalizer: when closing the valves of the single tanks or entire rows of tanks, or even when tanks are removed, the system is able to maintain constant water flow.



changing, thanks to a sensor positioned on the mechanical filter. Absolute safety is thus guaranteed.

All you need is a water supply and exhaust system and an electrical connection to have a single working station to manage the overall system.

The system features a back-up pump: in case of malfunction it is already installed and there is no need to store spare parts in the housing facility.

The system also has a cartridge filter (the operator can select the range of filtration, from 1 to 20 μm), and carbon-activated and acid-washed cartridges (thus not altering PH values in the system): before returning to the tanks, the overall amount of water re-circulating in the system is disinfected using a powerful UV-C lamp capable of delivering 200,000 $\mu\text{Watt/sec/cm}^2$.



All these parameters are controlled and monitored from the Touch Screen display. This easy-to-use soft-touch pad on the front door is a monitoring and management unit by means of which the quality parameters of the water may be set and constantly checked.

The temperature controller is also set with the same pad. Visual warnings help the user to manage the system properly: the XenopLus is the only system to feature an alarm related to the due time of filter

■ Marco Brocca, Aquatic System Market Manager

Ventiwheel

The Individually Ventilated Activity Wheel Cage



The use of IVCs is now consolidated in the field of biomedical research. In response to specific requests from the market, Tecniplast has now developed VentiWheel: the first product for activity studies that guarantees the same environmental quality as an IVC and can be individually ventilated through the simple positioning of a top, which is perfectly compatible with our IVC Sealsafe rack.

The wheel is the same as that in the Activity Wheel Cage, whose practicality has already been widely demonstrated. The new VentiWheel features two supports ensuring even smoother rotation of the wheel itself.

The cage comes with a stainless steel lid with a housing for the feeder, which can be extracted and washed without removing other parts of the cage. The lid increases the thickness of the cage body, so that the top is perfectly sealed, and it features holes to guarantee correct ventilation inside the cage.

The sensor to count the turns of the wheel is positioned on the lid without its top - if the top needs to be applied, the sensor must be mounted on the top itself. Once the sensor is removed, the cage is completely autoclavable.



■ Marco Brocca, Market Manager

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**E-mail interview with
Juan Martín-Caballero DVM, PhD.
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George Crowhurst,
Panorama Editor,
in Varese, Italy

G.C.: Firstly, could you please tell us something about yourself, your background and your current position?

J.M.C.: I graduated with a D.V.M. degree at the University of Madrid, where I also did my doctorate. I started specializing in Laboratory Animal Science in Spanish National Research Centres, (CSIC), in 1982. I was appointed Head of Laboratory Animal Services at the National Biotechnology Centre in 1992. I was then recruited by the Spanish National Cancer Centre, (CNIO), in 2001, as Head of the Laboratory Animal Unit where I designed the animal house, and supervised its construction and start-up.

It was also my job to generate Standard Operating Procedures and Policies governing the operations of the CNIO Animal Unit. I set up the Institutional Committee for Use and Animal Care (CEUCA) at CNIO, to evaluate all those research projects involving the use of laboratory animals. I am also in charge of health screening and welfare of animals in CNIO, and also manage the export-import process around the world on the basis of Material Transfer Agreements with other research institutions. Since the correct handling and care of the animals is a key factor in guaranteeing their overall welfare, as well as the quality of animal research, I have elaborated a short course to be followed by anyone working with animals at CNIO.

I have forged a number of collaboration agreements between CNIO and external research groups regarding phenotype characterization of genetically engineered mice, taking part in many research projects and submitting numerous scientific papers. These days, my main research line is Tumour Early Detection by In vivo Imaging systems and correlations with biomarkers in the blood.

I am a founder member of both SECAL (Spanish Society of Laboratory Animal Science) and ESLAV (European Society Laboratory Animal Veterinarians), and ad hoc AAALAC International consultant.



G.C.: Now please tell us something about the CNIO centre in Madrid - its mission, how big it is, what sort of activities are carried out etc.

J.M.C.: The mission of the CNIO is to conduct research with a high degree of excellence and to bring the very latest technology in the field of cancer to the benefit of the Spanish National Health System. With both goals in mind, strategic objectives for the CNIO have been established:

- To carry out research driving towards the discovery of new and effective diagnostics for cancer patients.
- To bring scientific breakthroughs into the clinic to ensure that the advancement is translated into reality for patients within our National Health System.
- To pass on CNIO developed technology to innovative companies.
- To create a new and efficient management system, breaking away from the traditional Spanish model.



The CNIO is one of the few European Cancer Centres to allocate resources to both basic and applied research in an integrated fashion, thus supporting the interaction of basic research programmes with those of molecular diagnostics and drug discovery. All our programmes benefit from excellent equipment, technology, and technical services.

The CNIO is actually housed in two separate buildings, with the capacity of a scientific staffing of 350 individuals. On the one hand, we have the old Victoria Eugenia hospital which has lain idle for the past decade, and has now been totally refurbished to house the basic research laboratories, the library and general offices. We then have a totally new building to house applied research, the Animal Facility Unit, and the underground parking lot. Despite this physical separation, interaction is lively between both camps, given that the other amenities - such as the seminar rooms, the restaurant etc - are shared by all.



The various research lines each have individual requirements which is why our building has been planned in such a way as to provide an infrastructure capable of supporting a wide range of research - the structural analysis of molecules (NMR, X-ray Crystallography), all types of molecular biology techniques, Microscopy (conventional, fluorescent, confocal, etc.), the latest technology available in the field of cytogenetics,

functional genomic (DNA chips), immunohistochemistry (Tissue Arrays), and the generation of transgenic mice. The SPF Animal Facility, one of the largest in Europe, boasts robotic cleaning equipment to guarantee homogeneous treatment and sterilisation. The Biotechnology Units not only offer their services to our researchers, but also ensure that the Centre has access to the very latest technology necessary to conduct research at the very highest level of excellence.

The CNIO has a total surface area of 32,000 m² of which more than 10,000 m² is dedicated to laboratory space, and 3,000 m² to the SPF Animal Facility.

G.C.: I know that you have recently introduced a degree of automation into your facility; can you tell us what were the crucial factors in choosing the type of equipment to install and what benefits you have derived?

J.M.C.: The Animal Facility Unit at CNIO is primarily responsible for the supply, husbandry and quality control of laboratory animals used by research programmes in experimental protocols and for assuring compliance with national, EU and international regulations and recommendations regarding the use and care of animals in research. The Unit has room available for up to 90.000 mice in its barrier area where Specific Pathogen Free (SPF) health status is assured through a comprehensive health surveillance programme. Currently, hundreds of genetically engineered mouse strains are being introduced into the barrier area by embryo transfer, and reared by foster mothers.



Daily operations and husbandry procedures are highly automated, with the use of robotic devices for all potentially harmful tasks (dirty bedding processing, cage and bottle washing and filling, etc.) to avoid associated physical and psychological hazards for personnel (since they are repetitive, mechanical tasks), biohazard and exposure to animal allergens that could lead to the development of professional allergy and possibly even asthma. These systems provide us with the highest productivity and quality standards in our washing and sterilising areas. Microbiological and environmental parameters are frequently monitored in animal areas. Bedding, water and cages are sterilized by autoclaving, the diet is irradiated. An air shower and sterile clothes are required for the personnel working under strict SPF conditions to enter the barrier area.



G.C.: What sort of caging do you have currently installed, and what benefits do you gain from using IVCs as opposed to traditional static cages?

J.M.C.: We have both static isolators and IVCs racks. The most important advantages in using IVCs are for the mice, since they prefer to remain longer in their cages with their pheromones. This is possible only with IVCs because you reduce at the same time the levels of injurious gases. The second important point is that they offer greater protection more efficiently than do static isolators to both mice and the operators who handle them.

G.C.: In terms of equipment, are there any improvements you can suggest, or is there any kind of equipment that you don't have but would like to have - any suggestions for those developing new products?

J.M.C.: Given the proven success of the MouseHouse, it might be useful to have IVCs of the same red colour and soundproofed cages to reduce stress in mice.

G.C.: Finally, what developments do you see in the not-too-distant future?

J.M.C.: I think that in the near future we will use fewer animals and their equipment will be more sophisticated, with many different sensors inside the cages to have real-time feedback of various physiological and microenvironment data from the mice. The emphasis will be on quality rather than quantity.



ISOCAGE: THIS IS PROGRESS!

What does it take to create a new product that meets the requirements of those who are going to actually use that product?

- First you need to know what the user requires, and this may even mean going beyond the user's own expectations or wildest dreams. You need interpretation.
- Then you need the skills to design and engineer that product to correspond to those requirements. You need technical expertise.
- After that you need to put the product through exhaustive tests and simulations. You need thoroughness and attention to detail.
- Later still you need to let the user "play" with the product to check that you really got it right. You need user involvement.

After each of the phases outlined above, you need to seriously consider the feedback you have received and engineer it into the product. You need to be interactive. When dealing with crucial equipment for the animal laboratory, this process requires a range of skills and a commitment that are not readily available.

The creation of the Tecniplast ISOCAGE is a real example of a group of dedicated people (users included) with a variety of skills working together to come up with a solution to make the operator's life both safer and simpler. The initial requirements are identified by a product manager in direct contact with users inside their own facilities during their daily work.

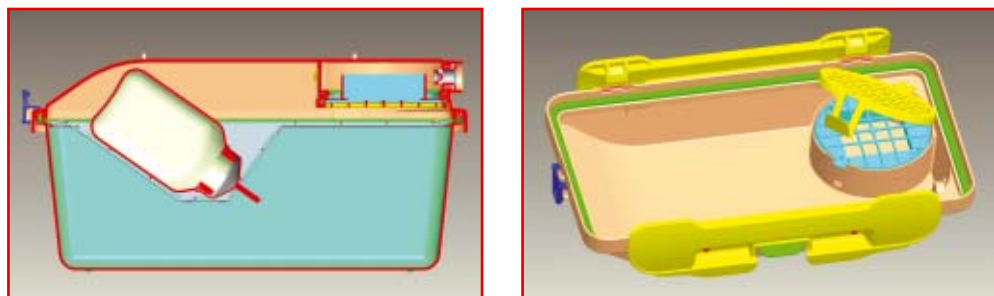
The feedback received requires scientific screening by an expert in animal husbandry and real lab conditions. The joint feedback of these two figures is shared with highly qualified technical staff whose experience ranges into other fields such as aeronautical and mechanical engineering. These people bring to bear the weight of their accumulated knowledge both in this specific field and in other sectors so as to ensure that the design of the product will meet and even surpass the expectations of the user. Thus the product takes shape, first as a 3D CAD model, then as a prototype, then as a sample product to be tested by real users in real conditions, and finally as a manufactured item to benefit a host of users.

This is how the ISOCAGE (and not only the ISOCAGE) came into being.

- What was needed was an ISOLATOR AT CAGE LEVEL working exclusively in negative pressure with dual Hepa filtration on the outlet as a protection for those working with human pathogens.
- It had to have the features of an IVC, be ergonomic in its design to facilitate the daily routine of regular users.
- It had to be far more compact than the traditional isolator and be able to accommodate caged animals under different protocols.
- Designers had to take into account that it might be moved from one area of the facility to another where local atmospheric pressure might vary.
- Above all, it had to be SAFE - no leakages and as far as possible crash-resistant in case of accidental dropping.

This was the challenge that the potential users, the product manager and the veterinarian identified and passed on to technical staff.

This sequence shows how the ISOCAGE was developed, with all its unequalled features, down to the tiniest detail:



3D drawings were prepared for a cage featuring an internal HEPA filter on the exhaust with the whole system working exclusively in negative pressure.



A stereo-lithography fast prototype was produced, followed by an intermediate moulded prototype. In this way, the whole team was able to actually touch the product and refine it to reach the Ideal Final Result.

The outcome was a system confining contamination to the smallest possible area - the cage itself.

With just one fan drawing the air on the exhaust side, negative pressure is guaranteed throughout the system. Even in case of fan failure, positive pressure is out of the question. Moreover, the cage may be moved to areas with differing ambient pressure without affecting the pressure inside the cage itself.



The internal HEPA filter ensures that exhaust air is purified - it also features an additional, inexpensive wafer-thin disposable HEPA filter (replaceable every cage change) that avoids any clogging of the main autoclavable HEPA filter.

The soft silicone gasket is hollow in section and features tiny triangular ridges on the upper side to guarantee maximum uniform pressure and thus hermetic sealing even after many autoclaving cycles. The gasket fits snugly and firmly into its housing thanks to the central ridge with ejection points at regular intervals used to squeeze the gasket in place and ensure that it cannot fall out.

Cage air-tightness is ensured by the special gasket together with two clips covering 4 contact blocking points for uniform pressure and yet ease of use - 2 hands, 2 clips! Lock buttons ensure that the cage will remain safely sealed even in case of accidental dropping, while the material of which the cage is made is highly impact-resistant.



The cage valves feature two O-rings to ensure a perfect hermetic seal both when the cage is on the rack and when it is removed.

After any opening of the cage, safe conditions can be restored by dunking it in a disinfectant solution - with the animals inside the cage.



The cage is securely locked into the rack by means of earthquake-proof runners.

The smooth inner walls of the cage present no chewable points.



The Air Handling Unit is attached to the rack, but may also be moved around thanks to an Uninterrupted Power Supply. Cage vacuum pressure has been checked to last at least 10 minutes after undocking from the rack, and this has been verified after 100 autoclavings.

■ George Crowhurst, Panorama Editor,
in collaboration with:
Gianpaolo Milite, D.V.M., M. Sc.
Paolo Tamborini, Isocage Market Manager
Giovanni Malnati, Senior Product Designer

GREAT SUCCESS OF ISOCAGE™ AT EBSA!

Tecniplast is once again pioneer in Europe in the development of new products for the scientific and medical research community, as was clearly shown by our success at EBSA, where we presented the ISOCage™, the first total-containment individually ventilated cage. Many veterinarians and scientists have acknowledged that ISOCage™ represents the cutting edge in bio-containment thanks to its innovative features:

- 1) HEPA filter on the exhaust valve;
- 2) total bio-containment;
- 3) ergonomics (the importance of this feature in a BSL3 environment can never be stressed enough).

A quantum innovative leap in biological research!



■ Paolo Tamborini, Isocage Market Manager

PRODUCT INNOVATION & ENHANCEMENT

THE VET'S CORNER

Healthy rabbits ... better science!

When considering laboratory animals, an aspect that has to be taken into account is their behaviour and physiology.

Rabbits are highly social animals and therefore their behaviour and welfare cannot be underrated when they are inside an animal facility. Rabbits attach a great deal of importance to their olfactory sense (which is highly developed in this species), as well as visual contact. Every member of the group has a social position within a hierarchical order in which the dominant animals have authority over the subordinates.

The hierarchy among males is of a linear type, with male A dominating B, which in turn dominates C.

For this reason, whenever possible considering the type of lead experiment, it is important to allow them to meet others of their kind.



The guidelines for accommodation and care of animals of Appendix A (European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes, CETS No. 123) says: "A raised area

should be provided within the enclosure. This raised area should allow the animal to lie and sit and easily move underneath, but should not cover more than 40% of the floor space. While the enclosure height should be sufficient for the rabbit to sit upright without its ears touching the roof of the enclosure". Appendix A speaks about from 45 to 60 cm of minimum height and from 3500 to 5400 cm² for the minimum floor area for one or two socially harmonious animals.

Also "Pens should contain structures that subdivide the space to allow animals to initiate or avoid social contact".

With this in mind, Tecniplast has developed equipment for rabbits that allows them to freely express their instincts. The cage is equipped with environmental enrichment with a pen for social interaction, visual and olfactory contact, and with a removable wall for single or multi-housing, and its sizes comply perfectly with the indications of Appendix A.



Furthermore, also accordingly to the same guidelines, the cages may be placed on a shelf that allows locomotive training, prevents skeletal problems, gives the recessive rabbit the chance to escape and hide away and finally allows the dominant rabbit to gain the best position. All this improves the well-being of the animals, they are less stressed and also the experiments can be carried out under ideal conditions.

Luigi Mazzagatti, Product Manager

DS100 CABINET



DS100 is a cabinet for allergen containment during rat cage bedding disposal, in some cases also used for rabbit trays bedding disposal.

It features two steps of pre-filtration and DOP-tested HEPA filters.



NEW URINE COLLECTION TUBE

A new optional urine collection tube has been developed for the metabolic cage for a single mouse: this urine collection tube (cat. n. 3600M019) is made for diabetic large size mice exceeding common urine production and it has a 33 ml capacity.



NEW ISOCAGE™ MINI

Tecniplast is pleased to introduce the new ISOcage™ MINI.

This product has been designed to complete the ISOcage™ family and to meet the need of having a small ISOcage™ unit when the autoclave is small, for small laboratories working with infectious diseases, for quarantine purposes and as a transport trolley, too.

It will have supply pre-filters and HEPA filter on the lower right-hand side; exhaust pre-filter and HEPA filter on the left, and in the middle the soft touch for setting.

On top of this trolley there will be the possibility of installing mini ISOcage™ racks of 8 or 12 cages. Those racks have 4 columns and respectively 2 or 3 rows of ISOcages™ and they are screwed on to the trolley structure. When you need to remove them for autoclaving cycles you unscrew them, and simply slide them out.



Code 2ISO08CP: the unit consists of a trolley equipped with twin fan motor blowers to create the depression inside the cages, pre-filters and HEPA filters for both supply and exhaust, removable mini rack for seven complete ISOcages™ + the Control Cage.

Code 2ISO12CP: the unit consists of a trolley equipped with twin fan motor blowers to create the depression inside the cages, pre-filters and HEPA filters for both supply and exhaust, removable mini rack for eleven complete ISOcages™ + the Control Cage.

Giovanni Tartaglia, Flow Division Manager

Augusto Talamona, Product Manager

Paolo Tamborini, Market Manager