

## DEAR READER,

At Ellegaard Göttingen Minipigs, we are pleased to note an increased demand for Göttingen minipigs. The advantages of using minipigs compared to other species are being recognized in more and more areas of biomedical research. One of the reasons the minipig is more accepted by researchers and regulatory agencies alike is the increased amount of published background data.

At the moment we are participating in an EU project named Rethink, co-funded by the European Commission under the FP6 Framework Programme. The objective of the Rethink project is to evaluate the potential impact of toxicity testing in the minipig as an alternative approach in regulatory toxicity testing that can contribute to the 3Rs of animal testing: Replacement, Refinement and Reduction. (For further details, please visit: [www.rethink-eu.dk](http://www.rethink-eu.dk)) We hope this project can help to clarify more areas of toxicity testing where the minipig is the best research model for predicting toxicity in humans.

The majority of Minipigs are sold for toxicity testing. In this area it is of utmost importance that the animals used are well defined. Minipigs from Ellegaard Göttingen Minipigs are well defined with respect to health and genetics (please see information about the latest health monitoring report on page 4). All of us at Ellegaard Göttingen Minipigs understand the importance

of high health status and genetic stability. We aim to maintain the high health status and improve the genetics in a way that does not compromise comparability with previously published data.

Although health and genetics are important, availability is also critical for our customers. With our latest expansion in 2003 we still have the production capacity to increase production and we regularly adjust production to meet the expected demand. This is a difficult task since it takes 7 to 9 months before an increase in the number of breeding sows leads to higher availability of 3 to 5-month old minipigs. We want to ensure our customers that we prepare well in advance of the next expansion of our production capacity.

Finally I would like to draw your attention to the free handling courses we offer to ensure stress-free handling of our minipigs. This is as important for the employees who work with minipigs as for the minipigs themselves because it improves the working environment and the validity of the results following the study. Both new and experienced customers are welcome to request these courses, which can be held either on your premises or at our facilities, the latter of which gives you an excellent opportunity to visit our breeding centre. We are always pleased to present our breeding centre to current or prospective customers.

Jens Ellegaard, Managing Director

### "HANDLING AND DOSING THE GÖTTINGEN MINIPIG" – NOW ON DVD

The handling and dosing of minipigs is essential for successful testing of compounds.

Stress not only inconveniences the animals and technicians during the procedures performed, but may also have a major impact on the results obtained.

Ellegaard offers "hands-on" handling and dosing courses where basic procedures of handling and dosing of the Göttingen minipig are reviewed.

In connection with these courses, we have realised that an instructive DVD is needed.

Therefore, we have produced a DVD that follows the same principles as the DVD "Handle with Care" and the video "Procedures with Care", both produced by the Institute of Animal Technology (IAT), which deal with the

correct handling and dosing of other laboratory species. (For further information on the IAT's DVD and video, please visit [www.iat.org.uk](http://www.iat.org.uk)) The aim of the DVD is to facilitate in-house staff training at research organizations. Ellegaard emphasizes that handling courses are still organized whenever required and that you are always welcome to visit our facilities for this "hands-on" instruction, guided by our highly qualified staff, who have years of experience in working with the minipigs. In this respect, we believe the DVD will be a useful educational tool and course supplement. The DVDs "The Göttingen Minipig: Handle with Care" and "The Göttingen Minipig: Procedures with Care" will be available to our customers who are using or planning to use minipigs. Release date: September 2006. If you would like a copy of this DVD, please send an email to [ellegaard@minipigs.dk](mailto:ellegaard@minipigs.dk)

Clean pigs for clear results



Minipigs

Biological products

Auxiliary equipment

Training & Courses

## ELLEGAARD GÖTTINGEN MINIPIG APS JOINS EU PROJECT

Ellegaard has joined the RETHINK Minipig Project. The RETHINK minipig project will address and cover important issues concerning the use of the Göttingen minipig as an experimental animal, primarily focusing on minipigs used in toxicity testing. The project will cover issues, such as

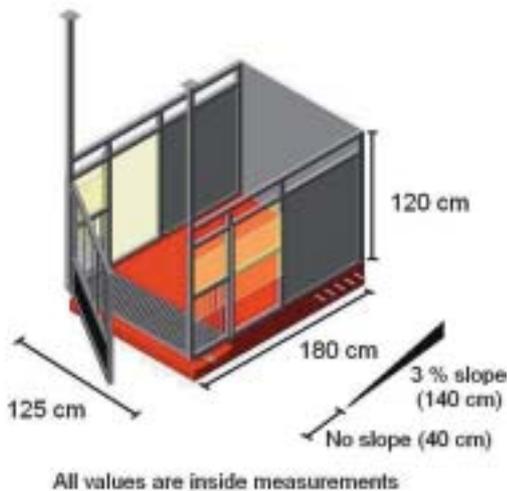
- how to ensure the welfare needs of minipigs in laboratories;
- the scope for application and development of the 3Rs by using minipigs;
- the potential role and best deployment of minipigs in toxicology testing strategies;
- the validity and added value of minipigs in regulatory toxicology;
- proposals for initiatives to fill knowledge gaps or “technical” gaps;
- implications for the development of new medicines and chemicals.

The project will result in a detailed report. For more information or to contribute to the project, contact the RETHINK project at: [coord@rethink-eu.dk](mailto:coord@rethink-eu.dk) The RETHINK Minipig Project [www.rethink-eu.dk](http://www.rethink-eu.dk)

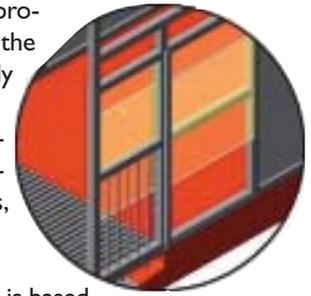
## BEST PRACTICE PEN DESIGN TOXICOLOGY

Ellegaard Göttingen Minipigs is often asked for advice on how to house Göttingen minipigs, yet there is no simple answer due to the wide variety of possible pen options. Each experiment has unique requirements, making it impossible to design one optimal pen for the Göttingen minipig.

### Pen for the Göttingen minipig



Therefore, we have designed a proposal which we choose to call the “Best Practice Pen”, for use only in the field of toxicology, however. Other types of experiments may pose altogether different sets of requirements, which would result in an altogether different pen design.



The design of the proposed pen is based on our experience in housing the minipig at our production facility, but the main input has come from our customers who have extensive experience in housing the Göttingen minipig. This information was gathered through a series of meetings and visits with these customers in 2004–2005.

In order to justify the investments needed to build a new animal facility (or to modify an existing one) the end product must be able to accommodate minipigs and dogs. Furthermore, it should be possible to use the proposed pen for both dogs and minipigs without having to modify the pen when alternating between the species. The proposed pen complies with EU requirements for housing minipigs.

## FLEXIBILITY AND ANIMAL WELFARE ARE PARAMOUNT IN THE DESIGN PROPOSAL

Layout and dimensions have been adopted to maximize the flexibility and usability of the pen, as well as to ensure a healthy environment for staff and animals alike. The area of each pen is 2.25 m<sup>2</sup>, one-fourth of which is a slatted floor and three-fourths solid flooring. The pen is 125 cm wide and 180 cm deep (interior measurements) and has floor heating. The solid part of the floor has a 3 % slope towards the aisle. The slatted floor is made as an insert and can easily be replaced with a solid floor insert.

Dog traps in the side walls enable two or more pens to be combined for group housing. More importantly however, the floor area of the two pens meets the EU's requirements for dog housing. Vertical bars allow physical (snout) contact between animals in adjacent pens. Physical contact can be prevented by lowering the sliding partition.

The design makes for easy maintenance and cleaning, both of which are important factors to consider in designing pens. Detailed information on the models available and the types and placement of drinking units, feeding troughs and environmental enrichment is available – please inquire.

If your company is planning to build a new animal facility or refurbish an existing one, we would be pleased to visit your facility and give a comprehensive presentation on the subject. This will give you the opportunity to consider the minipig requirements.

The development of the Best Practice Göttingen Minipig Pen is an ongoing endeavour, where there is always room for improvement. Therefore we would like to hear your comments and any lessons you have learned from housing Göttingen minipigs.

Send us an email at [ellegaard@minipigs.dk](mailto:ellegaard@minipigs.dk) and write “Housing, feedback” in the subject line.



### ELLEGAARD GÖTTINGEN MINIPIGS IS PLEASED TO INTRODUCE YOU TO TWO NEW PEOPLE IN OUR OFFICE.

As Trine Christensen is currently on maternity leave, her shoes will be filled during her absence by Kirsten Nielsen who is handling minipig orders and coordinating the transportation. Kirsten has been with us since primo March, 2006 and is fully up to speed with our ordering and transport procedures. Trine will be back in the office by early 2007, after which Kirsten will continue on a part-time basis for the company.

Niels-Christian Ganderup is our new scientific sales manager. He holds a master's degree in biology and is one of our scientific contacts who assist customers with scientific and technical questions. He participates in most of the exhibitions where our company is represented and is currently on the programme committee for the Safety Pharmacology Society.

### NON-SURGICAL MINIPIG CATHETERIZATION: USING THE ARROW CATHETER

Intravenous injection and especially serial blood sampling of the Göttingen minipig may prove difficult, since larger blood vessels, like the jugular vein, are not clearly visible and the ear veins are small.

Blood sampling is often performed by placing the pig in a V-trough to collect blood from the precaval sinus.

This procedure requires specially trained personnel to en-

sure that the pig is not stressed, yet the method is not expedient if frequent samples have to be taken from the pig over a short period of time.

Also, this method is not favourable if urine and faeces have to be collected quantitatively – in addition to the blood samples, and if the pigs have to be housed in metabolic cages during a study.

An alternative blood sampling or intravenous injection method is to implant a catheter surgically. Among the various types of catheters available is a specialized catheter known as Vascular Access Port (VAP), where the catheter is connected to a subcutaneously placed reservoir.

An implanted catheter may also be connected to an AccuSampler® to obtain samples without having to handle the pig.

One disadvantage of these methods is that the pig has to undergo surgery to identify and catheterize the chosen vein.

To avoid a surgical procedure, an alternative is to implant the ARROW® catheter, which also has the advantage that if the catheter clogs, it is easy to replace. This is done by introducing a new guide wire, removing the catheter and replacing it with a new catheter.

The Seldinger method was adapted for the minipigs by Preclinical Pharmacokinetics, Schering AG, Berlin, where the following procedure for implanting the ARROW catheter in the jugular vein of the Göttingen minipig has proven its success: [See the bottom of this page](#)

### ELLEGAARD GÖTTINGEN MINIPIGS STOPS MICRO-CHIPPING

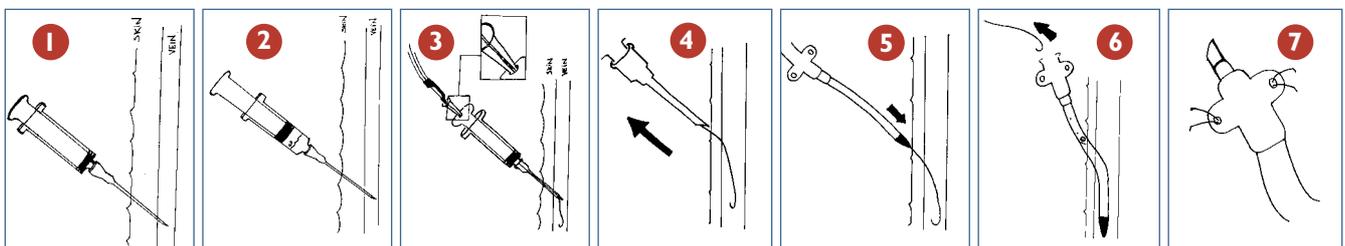
At Ellegaard, each pig receives an individual five-digit number shortly after birth. The last two digits of this number are used to identify the piglet by cuts in the ear (picture A). These cuts remain visible throughout the pig's life.

The piglet receives an ear-tag with the complete five-digit

### PROCEDURAL DESCRIPTION:

The pig is anaesthetized and placed on its back.

The procedure is carried out aseptically, i.e. the pig is prepared as for surgery: shaved, washed and disinfected.



1. An introducer needle with syringe (Arrow Raulerson Syringe) is inserted into the jugular vein.

2. Blood flash-back indicates that the catheter has been correctly inserted.

3. The spring guide wire is led through the syringe and needle into the vein, until the tri-band marker reaches the end of the syringe. The introduction of the spring guide wire should be possible without pressure. Otherwise the introduction should be finished before the tri-band marker is reached (the vein is too small) and it should be proceeded as described in the next step.

4. The syringe and insertion needle are carefully removed while the guide wire remains in the vein. After removal of the syringe it is helpful to widen the skin opening a little bit with a surgical forceps for easier access of the catheter.

5. The pointed end of the catheter is now guided into the vein via the guide wire and the catheter is pushed into the vein until the marker "8-10" (dependent on the pigs weight and size) is near the skin opening.

6. The guide wire is now removed, being careful not to change the position of the catheter in the vein.

7. One or two sutures are used to fix the catheter to the skin at the catheter clip. The catheter is also secured to the neck using tape.

The catheter is filled at least two times a day with 2 ml of Liquemin solution (500 IU) or the like. The catheter can remain open for a minimum of 14 days. If you would like further details on how to use the ARROW® catheter in the minipig, please email us at: [ellegaard@minipigs.dk](mailto:ellegaard@minipigs.dk).

number when the piglet is either moved to a multi-suckling unit at 14 days of age or when weaned (if the piglet is not moved to a multi-suckling unit).

Furthermore, a Sokymat transponder is implanted into the Gottingen minipigs to ensure that identification is possible even if a pig loses its ear tag.

A whiteboard is placed outside every animal room, showing where each pig is housed. A magnet on the whiteboard marks each pig. Whenever a pig is moved to another pen, the magnet is also moved. The moving of a pig is recorded electronically as well.

This makes it possible to know at all times in which pen a pig is housed.

It is highly unlikely that two pigs – housed in the same pen and identified by numbers ending in the same two digits – will each lose their ear tag at the same time. Should this happen, however, the two pigs in question will be removed from production and will not be sold for research purposes.

As a supplement, the Sokymat transponder was also implanted to make it possible to record data using a transponder-reader, followed by automatic transfer of recorded data to our computer system. This was to reduce the load of manual paperwork that has to be carried out by our staff. Unfortunately the Sokymat transponder has proven unsuccessful for this procedure.

As the above have rendered the transponder unnecessary, Ellegaard will stop the intra-muscular micro-chipping of pigs.

Ellegaard is now looking for another type of microchip, which will allow us to record data, such as weight, electronically. The new chip will be placed in the eartag, which will prevent the placement of the chip in the neck muscles and hereby remove any risk of interference with muscle samples sampled for pathology investigation.

In the future, transponders will only be implanted on request. Please notify us if you have any specific wishes for what the new chip should be able to provide of information, we will be happy to include this in our considerations when choosing our new microchip.

For further details or comments, please contact us at [ellegaard@minipigs.dk](mailto:ellegaard@minipigs.dk).

#### HEALTH MONITORING REPORT, SPRING 2006:

The Health Monitoring Report, spring 2006, has no new findings.

#### 2006 COURSES:

##### “BASIC COURSE IN TELEMETRY IN LARGE LABORATORY ANIMALS”

Date: 2–3 November 2006

Organizer: IMTC, The Netherlands

Course address:

Operating rooms of the Central Laboratory Animal Institute, Nieuw Gildestein Building, Bolognalaan 50, De Uithof, Utrecht, The Netherlands.

Course fee: EUR 1,000.00 (not including hotel accommodation and 19% VAT).

Please visit [www.intmtc.com](http://www.intmtc.com) for a complete description of both days and a course registration form.

Course description:

This large-animal implantable telemetry workshop will emphasise the hands-on learning of advanced surgical implantation techniques, including intubation technique. Course participants will learn to implant BP and ECG transmitters in pig models. A working telemetry system and computerised collection of data will also be demonstrated. The course reviews large-animal telemetry surgery techniques and the most recent approaches. The course will primarily emphasise the learning of practical skills and methods from experienced instructors. Prior experience in small and or large animal laboratory surgery is recommended.

Each two-day course is designed for a maximum of eight participants.

Please do not hesitate to contact us if you have any queries concerning this programme. On behalf of IMTC, DSI and Ellegaard Göttingen Minipigs Denmark.

Sincerely yours,

Dr Klaas Kramer,

Technical Director IMTC

Professor, Dr. René Remie,

PhD, Scientific Director IMTC

Handling courses

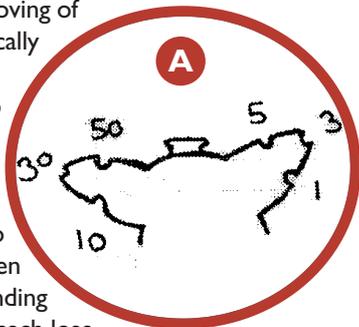
Date: organized as required

Course description:

Correct minipig handling is essential for obtaining a cooperative animal during the normal day-to-day handling and when performing experimental procedures with non-anaesthetized minipigs.

Handling courses are organized as needed and can be held at Ellegaard's facilities in Denmark or on your premises.

If you would like to schedule a handling course or get further details. Please email us at: [ellegaard@minipigs.dk](mailto:ellegaard@minipigs.dk) or call +45 5818 5818.



## REFERENCE DATA

In the last newsletter, Ellegaard Göttingen Minipigs called for the submission of pre-study data to be added to our reference database. Although we have received substantial amounts, we still need more. The reference data will be made available to all minipig users and can be viewed on our website ([www.minipigs.dk](http://www.minipigs.dk)) under "Background Data". The reference database is a work-in-progress and you are always welcome to contact us if you are looking for data which isn't on the website. Government organizations that deal with our minipigs from a regulatory perspective are also welcome to contact us regarding reference data. Earlier this year, Ellegaard Göttingen Minipigs supplied the USFDA with teratology data. The data was extracted from our breeding colony and covers the frequency of stillborn, syndactyl and polydactyl minipigs, the litter size of gilts (first time farrowers) and other parameters.

If you need information such as above you are welcome to contact us, and hopefully we can be of assistance. Much of this and other minipig data will be published in Michael Swindle's upcoming book – see BOOK RELEASES.

## MEETING CALENDAR 2006

Ellegaard Göttingen Minipigs will be presented at the following scientific meetings and exhibitions in 2006:

- European Teratology Society - 3-6 September, Abano Terme, Padova, Italy
- GV-Solas - 10-12 September, Freiburg, Germany
- EUROTOX - 20-24 September, Dubrovnik, Croatia
- Safety Pharmacology Society, 26-28 September, San Diego, USA
- European Society of Toxicologic Pathology - 27-29 September, La Grande Motte, France
- American College of Toxicology – 5-8 November, Palm Springs, California, USA
- LASA winter meeting, 29 November – 1 December, South Scotland

## BOOK RELEASES

Swine in the Laboratory: Surgery, Anesthesia, Imaging, and Experimental Techniques, Second Edition. Boca Raton, Florida, USA: CRC Press. Expected publication: December 2006.

A major contribution to disseminating knowledge about the Göttingen minipig is the upcoming release of Michael Swindle's updated and expanded version of his 1998 textbook Swindle, MM: Surgery, Anesthesia and Experimental Techniques in Swine, Boca Raton, Florida: CRC Press. In this new edition entitled: Swine in the Laboratory: Surgery, Anesthesia, Imaging, and Experimental Techniques, 2nd edition, the section on anaesthesia and perioperative care has been greatly expanded

and updated. All of the organ and system chapters have been updated with new techniques. New chapters include Toxicology (with focus on the Göttingen minipig) and Radiobiology, which were not included in the first edition. There will be an attached DVD with MRI, CT, and PET images performed in collaboration with the PET Centre and IEKF at Aarhus University, Denmark. A large number of tables with normal biological data, organ sizes and measurements of the Göttingen minipig and other swine will be included in an appendix in the new edition.

Shayne C. Gad: Animal Models in Toxicology, Second Edition, Marcel Dekker, 2006.

Zuhail Dinzer and Ove Svendsen have a chapter on toxicopathology in the Göttingen minipig.

## ARTICLES:

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