Refinements in telemetry procedures

Seventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement, Part A

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Preface

Whenever animals are used in research, minimizing pain and distress and promoting good welfare must be as important an objective as achieving the experimental results. This is important for humanitarian reasons, for good science, for economic reasons and in order to satisfy broad legal principles such as those stated in the European Convention and Directive on animals used for experimental and other scientific purposes (Council of Europe 1986, European Community 1986), the New Zealand Animals Welfare Act 1999 (New Zealand Government 1999), the United States Animal Welfare Act and Health Research Extension Act (see National Research Council 1996) and the UK Animals (Scientific Procedures) Act 1986 (Home Office 2000).

It is possible to refine both husbandry and procedures to minimize suffering and improve welfare in a number of ways, and this can be greatly facilitated by ensuring that up-to-date information is readily available. The need to provide such information led the British Veterinary Association Ani-

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mal Welfare Foundation (BVAAWF), the Fund for the Replacement of Animals in Medical Experiments (FRAME), the Royal Society for the Prevention of Cruelty to Animals (RSPCA) and the Universities Federation for Animal Welfare (UFAW) to establish a Joint Working Group on Refinement. This is under the chairmanship of David Morton and with a secretariat provided by the RSPCA. The RSPCA is opposed to experiments that cause pain, suffering, distress or lasting harm, but all members of the Working Group share the common aim of replacing animal experiments wherever possible, reducing suffering and improving welfare while animal use continues.

1 Aims of this report

This report is intended to help scientists, animal technicians, veterinarians and members of ethics or animal care and use committees to refine all aspects of telemetry procedures, from the project planning stage through to reporting finished research. It is published in two sections; this part (A) which is concerned primarily with procedures, and Part B (Hawkins *et al.* 2004) which addresses refinements in husbandry for rodents, dogs and non-human primates used in telemetry studies. It is strongly recommended that both reports are used together to ensure that suffering is minimized and welfare improved throughout these animals' lives.

Although this report was produced in the UK, it is intended for an international readership and refers to international legislation on animal use as well as to the UK Animals (Scientific Procedures) Act 1986 (A(SP)A). Some of the statements and recommendations are made with reference to 'cost/benefit analysis' which is critical in the implementation of the UK Act. Not all animal research regulations mandate a cost/benefit analysis, but it is an extremely important concept and one that many people and establishments employ, regardless of whether or not it is a requirement of their national legislation.

The report is focused primarily on 'costs' or 'harms' caused by procedures, but it is important to remember that these can be exacerbated or even exceeded by inadequate or unempathetic catching, handling, transport, husbandry, socialization and euthanasia. It is essential that all of these potential harms are considered in full and, similarly, that the benefits which may accrue from each project involving telemetry, including their potential application, should be subject to critical scrutiny. This report, therefore, aims to provide guidance for the scientists, technicians and veterinarians who will be conducting procedures on the animals involved and caring for them, in addition to those regulatory bodies that 'require' telemetered data (see ICH 2000) and those licensing authorities or ethics committees responsible for granting permission for research projects.

2 Telemetry and data logging

Biotelemetry is defined as the remote detection and measurement of a human or animal function, activity, or condition (Merriam-Webster 2002). This encompasses a broad range of techniques of varying invasiveness including video monitoring, non-contact thermometry, radio tracking and the use of internally or externally mounted remote sampling systems.

The present report focuses exclusively on refinements in the use of internally or externally mounted devices for transmitting or storing (logging) physiological data from experimental animals in the laboratory and in the field. This is because these techniques require specialist implantation surgery and/ or the fitting of external devices, which can cause suffering to animals in the short and long term if appropriate procedures and refinements are not implemented. The term 'telemetry' will be used to refer to both biotelemetry and data logging, as their impact on individual animals is broadly similar. For a useful review of the application of telemetry, see Kramer *et al.* (2001).

Telemetry is often presented as a refinement, in that it can reduce or eliminate stress caused to animals (e.g. by restraint), but it is vital to remember that telemetry, like all other procedures on animals, also needs to be refined. The impact of telemetry on animals in practice depends on the nature of the chosen technique and protocols—whether they involve surgery; the bulk (mass and volume) of the devices used; whether the technique necessitates husbandry that restricts the subjects' abilities to express a range of desirable behaviours; and, very importantly, whether the investigator has fully researched ways of refining both procedures and husbandry.

3 How to use this report

We recommend that this report (Part A) is read as a whole and in conjunction with its companion report (Part B, Hawkins *et al*. 2004), but it is also possible to use individual sections depending on the reader's particular requirements. The sections in Part A are set out in chronological order, beginning with the factors that need to be considered when making decisions regarding the justification for individual projects. The report then considers experimental design, choosing or designing a device and deciding on the method of attachment and device location before covering general refinements in surgical implantation.

Following surgery, the report considers the re-use of animals, the removing of devices and the potential for rehoming animals. Refinement issues associated specifically with telemetry studies using wild animals in the laboratory or field have been addressed separately in Section 11. The Working Group has also listed information that ought to be included when writing up studies involving telemetry, as a means of disseminating best practice. It is also vital that everyone involved in telemetry and data logging projects is well informed about new technological developments, as reductions in device size and new applications may enable further reduction of the impact of techniques on animals and improved experimental design. Section 13 in this report sets out how this can be done.

Part B to this report addresses husbandry refinements for rodents, dogs and non-human primates used in telemetry studies. It includes selection of suitable individuals, how to socialize animals, form stable groups and regroup animals following surgery so as to minimize aggression, and the welfare implications of long-term housing. This is an essential complement to Part A for those involved in rodent, dog or non-human primate use. Guidance for ethics or animal care and use committees based on the recommendations in Parts A and B is also available at www.lal.org.uk/telemetry/.

The Working Group recognizes that telemetry is a rapidly expanding and changing field, and stresses that it is essential to research emerging technologies and new information in *all* the areas covered by this report when planning projects involving telemetry. The approaches to refining experimental design and animal care will remain valid, however, as will the basic principles on the refinement of scientific procedures and maximizing information obtained from telemetry studies.

4 Harms and benefits associated with telemetry

The welfare of experimental animals involved in telemetry studies should be given a high priority, not only because animals matter as individuals in their own right, but also because good welfare is essential for good science. It is often assumed that transmitters will have no negative impact on the animals in whom they are implanted (Einstein *et al*. 2000, Murray & Fuller 2000), but this is rarely (if ever) the case. A comprehensive assessment of the possible harms and potential benefits associated with obtaining data by telemetry should be carried out for each proposed study as part of the overall cost–benefit assessment. Note that this should be reviewed throughout the duration of each project and should not be regarded as something that only needs to be done at the project planning stage. Section 4.1 aims broadly to set out potential harms (i.e. areas where telemetry needs to be refined), while Section 4.2 lists possible benefits (where telemetry could represent or facilitate a refinement).

Telemetry and data logging are relatively commercialized fields, and devices are frequently marketed as easily implemented and essential scientific tools. Telemetered data are also increasingly used to fulfil regulatory requirements—while not obligatory, it may only be the only way to provide data that fulfil the requirements of regulatory bodies (e.g. ICH 2000). It is therefore essential fully to consider the type of data required, its potential applications and scientific necessity, and to select the least invasive method of data acquisition that will provide meaningful and necessary results in each case. This should be assessed in depth by the appropriate local ethics or animal care and use committee for each project.

> All of the recommendations made in this report are intended to guide ethics or animal care and use committees as well as individual scientists, animal technicians and veterinarians. Additional guidance and discussion topics aimed specifically at ethics or animal care and use committees are set out at www.lal.org.uk/telemetry/.

Recommendations:

- **Make sure that there is a genuine scientific requirement for data obtained by telemetry or data logging; question regulatory requirements if necessary.**
- **Ensure that the welfare of animals on telemetry studies is given a high priority.**
- **Regard the assessment of the harms and benefits associated with telemetry as an ongoing process, not a single event—regularly review all of the issues set out in this report.**

4.1 Potential harms associated with telemetry

There are three key sources of harm associated with telemetry that can be refined to reduce suffering and distress:

(1) surgical implantation or attachment procedures;
(2) the physical impact of the device on the animal once it has been implanted or fitted; and
(3) distress induced by housing animals individually and by prolonged housing in the laboratory.

Issues 1 and 2 are the main focus of this report (Table 1 lists relevant sections), while 3 is covered in Part B. Further considerations for studies involving wild animals in particular are included in Part A and listed in Table 5, Section 11.

Recommendations:

- **Ensure that all the potential harms to animals have been set out as fully as possible for each project, that the potential for minimizing them has been fully researched, and that all possible refinements are implemented.**
- **Use Parts A and B of this report to think about the lifetime experience of each**

Table 1 Potential harms associated with the use of telemetry and report Sections that address them

• Anaesthesia or sedation	Section 8
• Surgical stress	Section 8
• Post-surgical pain and discomfort	Section 8
• Chronic postoperative discomfort and pain due to presence of the device (e.g. due to mass, dimensions or location)	Section 7
• Wound breakdown	Section 8
• Chronic adhesions; inflammatory lesions; seroma	Section 8
• Physiological stress and disturbance of energy balance due to the extra load imposed on the animal	Section 7
• Impeded movement, skin/fur/feather abrasion from harnesses, jackets and poorly placed devices	Section 7
• Individual housing due to undesirable attention from conspecifics to external devices and mountings; periods of isolation for experimental purposes	Part B*
• Prolonged housing in the laboratory due to reuse, especially dogs and primates	Part B and Section 9

*Hawkins *et al*. (2004)

individual animal used in telemetry studies and be aware of all the potential adverse effects (likely and unlikely) that they may experience.

4.2 Opportunities for refinement using telemetry

Potential benefits of telemetry are set out in Table 2. It is essential that these are as meaningfully, comprehensively and critically considered with regard to the potential harms to animals. In particular, it is important to ensure that all benefits are taken full advantage of wherever possible and that any associated drawbacks are addressed and minimized, so that animal welfare and scientific validity are improved and suffering is reduced.

Recommendation:

- **Consider using telemetry if it will reduce overall suffering, enable the use of fewer animals, or provide more valid, relevant data (without causing additional suffering)—but ensure that you do *everything* that you can to minimize discomfort, pain and distress.**
- **For ethics and animal care and use committees: ensure that the scientific benefits of each study, including the reasons for using telemetry, have been fully set out and weighed against all of the potential harms to animals.**

4.2.1 *Refining procedures using telemetry*

It is very widely recognized that telemetry can reduce stress to animals because it reduces or eliminates the requirement for external instrumentation, restraint or tethering. Telemetry can also provide objective biological evidence of animal well-being, such as variations in heart rate, blood pressure and body temperature, that may reflect acute or chronic discomfort, stress, distress, pain and fear. This applies to both experimental and husbandry procedures (e.g. Duke *et al*. 2001, Harkin *et al*. 2002). In addition, the return of variables such as heart rate to normal circadian rhythms can be used as indicators of physiological recovery and readiness for procedures. It may also be possible to use telemetered variables such as body temperature to help set humane endpoints in toxicity tests or disease models, e.g. to detect small changes in body temperature that signify the terminal stage of a disease (Kort *et al*. 1997, 1999, Vlach *et al*. 2000). Animals should benefit from this potentially increased level of monitoring wherever possible unless, for example, this would result in protracted periods of individual housing (but see Part B).

The Working Group considered whether animals should be implanted with devices specifically for assessing and revising endpoints, or whether this should only be an incidental benefit of instrumentation that is a necessary part of the project. It was concluded that, on a case-by-case basis, any adverse effects associated with implantation purely for monitoring purposes should be considered against the potential to refine the endpoint and the predicted level and duration of suffering that this will prevent (see Kort *et al*. 1999). Animals should not be implanted with telemetry devices that are scientifically unnecessary to the study unless it is certain that they will benefit, and the balance of harms and benefits will need to be fully and

Table 2 Potential benefits of telemetry

- Better quality data due to reduced stress and physiological disturbance (once animals have recovered from device attachment or implantation)
- More relevant data, as animals are able to behave more normally and even range freely, e.g. in radio tracking or data logging studies
- Chance of capturing occasional and transient events over a long period, e.g. abnormal heart rhythms
- Reduced physiological and psychological stress, since animals are not restrained or attached to external apparatus
- Reduced movement artefacts, e.g. due to exteriorized cables
- Possible reductions in the numbers of animals required due to more and better quality data

critically considered in each case by the scientists as well as by the relevant ethics or animal care and use committees.

Recommendations:

- **Think beyond using telemetry solely to obtain the scientific data that you require—use it to assess and monitor animal well-being and to refine procedures and husbandry wherever possible.**
- **If telemetry is used in toxicology or disease studies, regularly review the data to see whether there are any indicators that would enable humane endpoints to be further refined.**

4.2.2 Using telemetry to refine housing and care

Group housing is an important need for social species and should be provided wherever possible to improve both animal welfare and scientific validity. The development of fully implantable telemetry devices has made it possible to group-house animals and allow them to interact with others, because there are no externally carried backpacks or skin buttons that could be damaged by conspecifics, or in the case of behavioural studies that might change their behaviour. Part B provides essential guidance for achieving stable group housing for rodents, dogs and non-human primates (Hawkins *et al*. 2004). However, the greater invasiveness of the surgery necessary to fit total implants increases the severity of procedures. This is something that must be considered when performing a harm-benefit assessment of proposed studies (see guidance for ethics or animal care and use committees, www.lal.org.uk/telemetry/).

Implants can also be used to evaluate the physiological effects (and possibly levels of stress) due to routine husbandry, e.g. cage changing (Duke *et al*. 2001, Harkin *et al*. 2002). The information obtained can be used to refine husbandry and reduce stress, for example by helping to determine the least stressful time of day for husbandry (or experimental) procedures (Kramer *et al*. in press).

Recommendations:

- **Ensure that the potential to group-house animals is given sufficient weighting when deciding on the degree of invasiveness for each study—social contact is very important for many species and individuals.**
- **Ensure that telemetry is used wherever it will represent or facilitate an overall refinement.**

4.2.3 The potential for reduction

Telemetry improves data quality and quantity, which can lead to a reduction in the number of animals required for each study (e.g. Kinter & Johnsen 1999). In toxicology and pharmacology, telemetry may also be able to identify dose-limiting effects of a compound evidenced by subtle changes in blood pressure or heart rate, so that higher dosing studies are not required.

However, reducing animal numbers can also increase animal suffering, and it is important to be aware of this and make sure that it does not happen. For example, as implant miniaturization has progressed, sensor functionality has increased such that individual devices may increase in size because more parameters are being measured. Larger batteries may be required, which also makes devices more bulky. These devices will be heavier and require more invasive surgery to implant them.

Recommendations:

- **Ensure that animal numbers have been reduced as far as possible by taking the better quality and quantity of data obtained using telemetry into account when designing experiments.**
- **Recognize that there can be a 'trade off' between reduction and refinement, e.g. where fewer animals are used but devices are more bulky or complex. Consider the impact on each animal and do not reduce numbers at the expense of individual suffering.**

4.2.4 Data quality

Telemetry techniques can provide better quality data in two ways. The first benefits science in that the results obtained can be more meaningful and representative of an unencumbered animal (e.g. Schnell & Wood 1993, review in Brockway & Hassler 1993). This *can* also directly benefit experimental animals if it means that procedures are less stressful and fewer animals can be used in each experiment. (It should be noted, however, that implanted telemetry devices can also have an impact on results, for example by altering dose–response curves (Einstein *et al*. 2000).)

The second way primarily benefits science in that telemetry can be used to conduct studies that would previously not have been feasible. For example, many investigations of cardiac responses in animals undertaking behaviours such as diving could not reliably be carried out without implantable devices. While benefits for animals can also accrue from these studies (e.g. if they inform veterinary medical progress or environmental policy making), these benefits may not be direct. Sometimes the only immediate benefit is the addition to human knowledge, and so the justification for using telemetry in such studies is quite different from the justification for using the technique to reduce stress and/or animal numbers in experiments that would have been conducted in any case.

Recommendation:

- **Ensure that benefits are defined and interpreted from the animal's point of view as well as from a scientific aspect when making decisions on justification and necessity.**

5 Legal issues

There are three main categories of law that must be complied with when planning telemetry studies: (i) laws regulating the use of animals in scientific procedures; (ii) laws regulating field studies on animals, including releasing them; and (iii) regulations applying to the use of electronic equipment and radio frequency emissions. All of the relevant legal implications must be researched and considered in full when planning projects involving telemetry. For more detail on legal issues, see www.lal.org.uk/telemetry/.

Recommendation:

- **Research thoroughly all relevant laws relating to animal experiments, taking wild animals for scientific purposes, and electronic equipment. Make sure that all necessary permits have been obtained.**

6 Experimental design

There are two aspects of experimental design that have welfare implications and therefore need to be carefully considered, alongside expert advice from statisticians and device manufacturers' technical support staff, as appropriate. First, data need to be carefully managed to ensure that animals are not used unnecessarily. Second, the layout of animal accommodation and arrangements for the acquisition of data should not compromise the welfare of the animals being used.

6.1 Data and sampling

Telemetry techniques can generate extremely large amounts of data. Adequate resources in place to handle the data effectively and review them regularly are essential, to ensure that the experiment is proceeding as planned and that the system is operating optimally. Input from a statistician at the experimental design stage will almost certainly be necessary to set up strategies for effective data management and data reduction, including sampling and staging protocols and selecting appropriate data management software (Festing *et al*. 2002). It may be advisable to conduct a pilot study and collect some representative data to ensure that data management will be adequate. If studies are not properly controlled, problems with experimental design may not be effectively detected and this could result in animals being used unnecessarily, or data missed, not used or wasted.

Once data are stored, a suitable program that will allow editing to remove unwanted or incomplete data (e.g. 'searching signals' that occur when the animal is out of range) is required. If data such as 24 h heart rate or blood pressure are generated continuously, then it may be only necessary to use data from, say, the first 5 min of each hour or to note deviations from predetermined limits. Programs that facilitate easy access to the required sections of the data are essential. It is also vital to note that important data may be missed through 'number crunching', so the trade off between rapid data management and the risk of incomplete data must be taken into account and data should not be discarded.

Timing of data collection is also crucial. For example, activity counts may be more meaningful during a dark, rather than light, phase for nocturnal animals. When several parameters are simultaneously recorded, the software needs to be able to keep an accurate time function, especially if two separate techniques are used e.g. telemetry and video. Variables such as heart rate and activity may also need to be correlated and it is vital to do this continuously as studies progress, to ensure that the experiment is still working, avoidable suffering is not being caused and the animals' time is not wasted.

Recommendations:

- **Obtain expert advice on data management, statistics and software at the project planning stage.**
- **Make sure that data are regularly reviewed and interrogated—do not let projects 'run away'.**
- **Investigate protocols for data reduction and 'number crunching' but do not risk losing important data.**
- **Consider animals' time budgets when selecting data sets for analysis; make sure that behavioural data are accurately correlated with physiological data wherever necessary.**

6.2 Physical arrangement of hardware

The location of telemetry systems in relation to housing should be given careful thought to ensure that animals have a good-quality environment, including social housing, but data are not lost. Stress to animals should be minimized by considering their usual behaviour patterns within the experimental pen or cage and positioning antennae where animals are likely to spend most of their time or perform the behaviour(s) under study.

As an example, where animals are required to perform tasks using specialized apparatus (e.g. non-human primates using a touch-screen computer), the equipment can be positioned in front of an extension to the holding pen or cage. This has two advantages; first, the animal does not have to be captured and moved for trials and second, the animal can choose to sit by the apparatus and 'work' when s/he wants to (Pearce *et al*. 1998, Crofts *et al*. 1999). With the receiving antennae positioned under the extension, telemetered data are only collected when certain conditions are fulfilled, i.e. the animal is 'working'. When the animals are not within this area a 'searching signal' is recorded, which is easily identified and removed by software programs during data analysis.

Thoughtful positioning of hardware can also facilitate visual contact between cages or pens. For example, when using devices that all transmit on a single frequency only one animal within each cage or pen can be monitored at a time. However, the transmission distance may be short, so that animals can be pair-housed (with one animal being implanted, or both with devices that can be switched on *in situ*) and cages placed close together. Using this system, pairs can see animals from different cages and recordings can still be made from all cages at the same time within one room. The short transmission distance will not interfere between cages, but only one individual from a particular pair can be monitored at a time.

By contrast, if continuous recording is required over long periods, such as 24 h cardiovascular monitoring, then it will be necessary to place receivers over most of the pen or cage area. If this is a large pen with group-housed animals then data will only be available from one animal at a time. Future developments in telemetry will allow either multiple animal recording by use of different frequencies, even in devices suitable for rodents, or the remote or programmed switching on and off of transmitters.

Recommendations:

- **Carefully plan housing and hardware to maximize the potential to group- or pair-**

house animals and provide environmental stimulation.
- **Consider equipment configuration to achieve experimental goals yet minimize stress, e.g. locate antennae in response to animals' behaviour and preferred resting places.**

7 Selecting or designing a device

The primary physical impact of a device on an individual animal will depend upon the relative size and mass of the device, its shape, the nature of the material from which it is made, its site and the method of attachment or insertion. It is vital to monitor, record and report any adverse effects associated with any of these to help others refine their protocols (Section 12). Technical problems are also an ethical and welfare issue because failure of an implanted device may mean the waste of an experimental animal's life before any research objectives have been achieved. It is best to purchase devices from commercial suppliers with an established support infrastructure where possible, as these are more likely to have a known track record and it is easier to predict whether they will fail. It will also be possible to ensure that all materials are high quality, *biocompatible* and can be (and are) sterilized effectively without compromising performance.

Decisions about acceptable failure rates need to be made on a case-by-case basis. It is essential to record device failure rates and investigate the reasons for failure, liaising with suppliers as necessary. Failure rates will depend on the nature of the device and its application, but as a general rule the Working Group suggests that a 10% or greater failure rate should be taken extremely seriously and should instigate a review of experimental techniques, manufacturers and suppliers.

Recommendations:
- **Limit technical risks by purchasing tried and tested equipment from a commercial supplier wherever appropriate.**
- **Monitor device failure rates and fully evaluate reasons if they become unacceptable—always provide the supplier with feedback.**
- **If your device failure rate reaches 10%, review both techniques and your telemetry supplier immediately.**
- **Research *and report* both optimal and inappropriate device shapes, dimensions, locations, attachment protocols, etc. in the scientific literature.**

7.1 Mass of the device

Adding extra mass to animals' bodies can have a significant physiological impact and cause discomfort and distress, particularly in small species such as rodents. In the short term, changes in body mass and behaviour following implantation surgery in mice indicate that well-being is impaired during the week following surgery, not only due to surgery but also to the mass and volume of the device (Baumans *et al*. 2001; BALB/c and 129/Sv strains).

The device mass that mice are expected to tolerate is disproportionately large in comparison with other species, which the Working Group believes is a serious welfare issue. Some strains may not be large enough to accommodate the device chosen for a study, and failure to take this into account and obtain expert advice when planning projects could lead to serious avoidable suffering and wastage of animals' lives. For these reasons, the justification for any biotelemetry study using mice should be subject to particular scrutiny. The potential to use passive transponders, which are lighter than devices with batteries (e.g. 1.6 g as opposed to 2.7 g), or totally non-invasive systems for mice should also be fully explored (see Section 7.4.1). At the time of writing, systems are becoming available that can record ECGs from conscious mice via recording platforms without restraint or implanted devices (e.g. www.mousespecifics.com)[1].

In the longer term, there is also evidence to suggest that mechanical loading may contribute to the regulation of body mass in some circumstances. For example, in wild-type deer mice (*Peromyscus maniculatus*) there is a significant and sustained loss of

[1]While such systems do not require surgery, being placed on the recording platform is likely to cause stress to mice. It is therefore important to habituate mice to the recording procedure and to make them feel as safe and secure as possible on the platform.

tissue mass that varies directly with the mass of the implant (Adams *et al*. 2001). The health and welfare implications of this are not known, but it is important to note that adding extra mass could, in some species, alter the 'set point' for body mass in the long term. This is especially important when using wild animals, particularly in the field.

Any device should therefore be as light as possible, but is difficult to set out general principles on suitable device size and/or mass. It is an oversimplification to assume that an implant of, say, 5% of body mass would have the same welfare impact in all animals regardless of body size (see Murray & Fuller 2000). Device mass is also sometimes compared with the mass of a mature egg in the case of a bird or reptile, or the mass of the offspring or litter at the end of gestation in the case of a mammal. The Working Party does not believe that it is necessarily acceptable to implant or attach a device that weighs the same as a mature egg or litter in or onto an animal, as pregnancy and egg development happen gradually so that the animals' physiology adapts to the extra mass (and, of course, neither occur in males).

It is also important to consider the effects of device mass on the energy costs of travel (e.g. Croll *et al*. 1992, Ropert-Coudert *et al*. 2000). It can be calculated (see Calder 1984) that the extra travel cost of carrying a device weighing 10% of body weight would be about 6% in mammals and 7.5% in birds. Using estimates of the distances travelled daily, it is possible to calculate the likely increment in daily energy requirement associated with transport of devices of known mass (see Croll *et al*. 1992). This will help to predict possible impacts on foraging time, but there are likely to be other implications for animals, for example reduced food delivery to young (Murray & Fuller 2000). Such considerations are relevant to the assessment of the welfare impact of telemetry equipment used in wild animals in the field (e.g. Culik & Wilson 1991).

Finally, and especially for wild animals, it is essential to take behaviour and adaptations to significant life events such as breeding fully into account. For example, some species of seabird rapidly lose body mass after their chicks have hatched, in what is believed to be an adjustment to optimize flight efficiency (Croll *et al*. 1991, Gaston & Perin 1993). Implanting a data logger could, in some cases, replace a significant proportion of body mass that had been lost for an adaptive purpose. Further tissue mass may be lost to compensate for this, which could have impact on the ability of birds to rear their chicks and also affect the scientific value of any data obtained.

Recommendations:

- **Think carefully about the mass of the device that you want to use and its potential impact on the intended study species, including its behaviour.**
- **For mouse studies, make sure that the chosen strain is large enough to implant with the device proposed for the study—it is absolutely essential to consult widely on this.**
- **Use passive transponders for mouse studies wherever possible; research the status of non-invasive systems.**
- **Question protocols that make arbitrary statements about percentages of body mass, or about masses of pregnancies or eggs.**

7.2 Shape and dimensions

The size and shape of the device must avoid or minimize any compromise of the normal physiological function or welfare of the animal in any way. Even when the relative mass of a device may not cause discomfort or pain *per se*, trauma, abrasion or prevention of normal function can occur if the device is of an inappropriate shape or incorrectly fitted (e.g. see Gedir 2001). For example, a 120 mg temperature transponder measuring 2.2 by 14 mm may represent only 1% of the mass of a 3-week-old inbred mouse, but would be likely to cause discomfort and interfere with normal movement and posture wherever it was implanted.

The length of devices may be an issue in adult animals such as rodents or marmosets who curl up to sleep, and it is also essential to avoid placing pressure on the bladder, liver or diaphragm when animals assume resting or sleeping postures. Where external devices will be attached to running, flying or diving animals, it is essential to minimize drag. This includes reducing the frontal area of the device, streamlining its shape and ensuring that it is attached in an appropriate location so as to smoothly extend the contours of the animal (see Obrecht *et al.* 1988, Bannasch *et al.* 1994). It is especially important to consult with experts and to search the literature for guidance on device shape and dimensions.

Recommendation:

- **Think about the physical conformation of the device and its potential to interfere with the full range of postures of the species.**

7.3 Location

The primary factor to consider when deciding on location is that device weight can cause discomfort and pressurize adjacent tissue. Although subcutaneous implants are generally well tolerated by rodents, large subcutaneous implants in any species can result in necrosis of overlying skin, leading to infection, dehiscence and sinus formation. It is preferable to site large implants in a body cavity where possible (e.g. the peritoneal cavity), between muscles or deep into a layer of fat, separating the device from the overlying skin. This helps to prevent seromas or pressure necrosis. However, note that pressure applied to the peritoneum can be very painful, so devices should be anchored to the parietal (not visceral) peritoneum. In or near the gut, pressure may cause an obstruction or perforation of the bowel (e.g. Broadhurst *et al.* 1996) or even pass into the gut lumen and leave the animal *per rectum* (A. J. Webb, personal observations in the pig). Experience has shown that devices located intraperitoneally in primates are generally well tolerated, provided that they are well placed and attached so that the intestine cannot become entwined. Subcutaneous implants, other than small transponders, are not suitable for primates.

In all cases, the device should be 'balanced' in the animal as much as possible as a unilateral load can lead to device slippage and postural problems. Both normal and post-operative behaviour of animals should be taken into consideration, including lying positions and scratching and grooming actions. Devices should be unaffected by limb movement during locomotion and should not restrict it. Thought should be given to the animals' centre of gravity when walking, running, flying, swimming or diving, if and how this moves location, and how devices can be positioned so as to minimize impact on the animal's posture and equilibrium. For example, devices should be placed between the scapulae in flying birds (Obrecht *et al.* 1988) and attachment to the caudal part of the body may impede thrust generation in animals such as fish, dolphins and seals (Bannasch *et al.* 1994). For semi-aquatic species there may need to be a compromise in practice between positioning devices so that drag is reduced, yet animals can maintain their balance on land (Chiaradia *et al.* 2003).

In fast-running mammals such as many canids and equids, the viscera accelerate and decelerate markedly with every stride and any implanted devices will move with them. This could cause pain and even tissue damage if location or attachment is not appropriate. As another example, male dogs 'cock' their legs to urinate, which may result in implants in the flank pocket or femoral artery catheters becoming dislodged. This can be avoided by placing the transmitter body in the inguinal region, ensuring that the pocket created for the device is not too large and that the catheter is long enough to permit normal behaviour (see Section 8.1.4). Careful observation of animals, a literature search and consultation with colleagues may all be necessary to position devices correctly.

Recommendations:

- **Think carefully about the potential of a device to irritate or damage adjacent tissue and make sure that it is appropriately sited and anchored.**
- **Make sure that the device will not interfere with exercise or posture, including sleeping.**
- **Monitor behaviour and appropriate physiological parameters to ensure that**

the physiological burden has been minimized.

7.4 Attachment or implantation?

Telemetry devices may be totally external, totally implanted or combine an implant that is connected to an external device. Each technique has advantages and disadvantages that will need to be carefully considered when planning a project (see also Kramer 2000, Table 1 pp 13–15) and both have the potential to cause severe avoidable suffering if carried out incompetently or using inappropriate methods. Animals may appear to recover physically and psychologically from any pain and distress due to inadequate technique, but causing avoidable suffering is ethically unacceptable.

From the animals' point of view, the ideal system would allow social animals to be housed in stable, compatible groups (see Part B) and to present a minimal risk of infection, and would not be interfered with by the subject or conspecifics. In practice, this ideal may have to be balanced against experimental requirements.

Recommendations:

- **Consider external or internal devices (or a combination of the two) from the animals' point of view, paying regard to individuals' life histories, normal behaviour of the species and the nature of the data required.**
- **Aim to use techniques that will permit as broad a range of desirable behaviours as possible.**

7.4.1 Total implants

Total implants[2] offer the potential benefits of low infection rates since no devices such as buttons or cables breach the integrity of the skin; freedom from interference by the subject; the possibility of group housing by preventing interference from other animals; and reduced care and maintenance requirements since there are no cutaneous exit sites (e.g. skin buttons) that would otherwise need regular attention. There are, however, a number of disadvantages and limitations associated with total implants.

- *Batteries can run down or fail*. Battery depletion is a significant problem for totally implanted telemetry devices, as *in vivo* replacement is generally impossible. Power consumption can be reduced if devices can be switched on and off *in situ*, so such devices should be used where possible to reduce animal numbers. Recharging batteries may be possible if devices have exteriorized cables, but this can lead to local heat generation. Recharging batteries more slowly can reduce this, but more prolonged restraint will then be required and this may cause distress.

  It is likely that future devices will have implantable, self-sealing connectors to permit battery replacement without the need to explant and replace the other components. This will require a surgical procedure, so consideration should be given to placing the battery pack in a superficial site so that the extent and invasiveness of surgery is minimized.

  Passive transponders that transmit temperature, gross motor activity and heart rate are available, and the potential to use them should be investigated on a case-by-case basis (see Kort *et al.* 1997). Passive transponders do not require batteries or refurbishment, so they are smaller than battery-powered devices. Some can also transmit characters that can be used to identify particular animals, facilitating group housing. Two disadvantages are that: (i) passive transponders have a relatively short transmission range, so they may require larger receivers or receivers to be placed very close to animals which can be stressful for them; and (ii) they cannot, at the time of writing, transmit signals that require relatively frequent sampling such as ECG waveforms or blood pressure.
- *The signal may not be strong enough*. In the case of rodents housed in conventional cages, an antenna covering the floor

[2] We define total implants as those where there is no breach in the animal's skin once the device has been implanted, i.e. all incisions are fully sutured and there are no skin buttons or other external attachments that pass through the skin.

area of the cage can be effective in ensuring good reception. For large animals such as dogs who require larger housing, careful placement of antennae and perhaps the use of multiple receiving antennae are required to ensure good reception and complete coverage of an animal's living area.

- *Access for* in vivo *calibration is generally limited or impossible*. Calibration has to be carried out at the time of implantation and also at explant wherever possible.

Recommendations:

- **If using total implants, carefully consider how battery life could be prolonged.**
- **Research the latest developments in passive transponder technology and battery replacement and calibration *in vivo*, to see whether protocols could be refined.**

7.4.2 External devices—jackets and backpacks

In the laboratory environment, external devices for telemetry are usually attached to the animal in a jacket equipped with pockets to contain the respective components; for field studies see Section 11.2. Jackets have the potential to cause distress and the duration of the use on individual animals should be limited based on clinical judgement and known growth rates where applicable (NB: thermoregulation studies preclude the use of jackets).

Jackets or backpacks may be purchased commercially from a variety of manufacturers or may be homemade. Suitable materials include denim, polyester mesh or fabric and Lycra™ (Lycra™ is very well tolerated by dogs), with fastenings of lacing, zip fasteners, 'hook and loop' or Velcro™. Jackets must be hard wearing and each animal should have at least one spare for cleaning and repairs. Care must be taken with cleaning, as some materials (e.g. cotton) may shrink and residues of some detergents can cause dermatitis. Jackets must always be totally dry before use.

Animals should be carefully selected and trained to tolerate jackets before any surgical procedures are undertaken, beginning with 15 min and leading up to a few hours or however long the experimental protocol requires. This can greatly improve the animals' acceptance of their jackets and reduce stress during studies. Working with breeders and suppliers to ensure that animals destined for studies involving jackets become habituated and trained to accept them is also an excellent way to reduce any distress and potential wastage of animals.

It is also important to ensure that each jacket fits the animal snugly and that loose or tight areas are avoided. Jackets may be either customized to fit individual animals or designed with sufficient adjustment and elasticity to allow for normal movement and growth. Locations of pockets and openings to accept devices and cables also need to be considered. Before surgery, the jacket should be very carefully checked on the conscious animal for precision of fit and the locations of cable exit sites or connector buttons should be marked on the animal's skin. The animal should be conscious so that the limbs are positioned correctly and so that the potential for the jacket to impede movement can be checked. It may be necessary to sedate some primates for the sake of their own welfare (to reduce distress) and human safety.

Jackets should be applied early in the working day to permit observation and detection of any problems. Animals with jackets should be checked at suitable intervals for any complications, particularly skin soreness or abrasions. This is especially important where dogs are fitted with full jackets, as these can lead to hind leg abrasions. Pigs will always interfere with one another's jackets, and dogs can also damage jackets (often by accident) so it may not be possible to group house them. In such cases, the possibility of pair housing should be fully explored before isolating animals. For individually-housed individuals, the presence of animals of the same species in neighbouring pens and provision of environmental stimulation are both recommended to shift animals' attention and reduce the chance of boredom and self-interference with jackets or attached devices.

The use of noxious substances (e.g. clove oil or Bitter Apple^{TM}) on jackets to deter interference is not recommended. Doughnut-shaped collars that attach to the collar area of the jacket in dogs may be helpful in preventing damage to jackets without overly restricting the dog's movement, but note that these collars can cause significant stress and should not be routinely used. It is also absolutely essential to check for the presence of infections that could be causing irritation before fitting 'doughnut' collars. An effective selection and training process before fitting and appropriate environmental stimulation afterwards ought to prevent undesirable behaviours when animals are wearing jackets.

Recommendations:

- **Limit the use of jackets and backpacks as far as possible—these can cause distress.**
- **Ensure that jackets are individually fitted to animals before surgery so that they will not impede movement.**
- **Consider liaising with breeders or suppliers so that animals can habituate to jackets from an early age.**
- **Apply jackets early in the working day to detect any problems.**
- **Group-house animals wherever possible, using Part B to this report as guidance. If this is not possible, house conspecifics in neighbouring pens and provide extra environmental stimulation.**
- **Only use 'doughnut' collars as a last resort—try to prevent physical interference by appropriate selection, training and husbandry.**

7.4.3 Internal devices with exterior components, including skin buttons

Implanted transducers with cables or connectors that pass through the skin to an external signal processing device and battery pack permit the monitoring of multiple physiological parameters and the use of transducers with high power requirements. Such systems allow for battery changes, fault finding and for easier modifications, refinements and upgrades during the *in vivo* phase of a study if required. The use of externally attached components may limit the potential for group housing, however, as the animal may interfere with the devices or they may affect the behaviour of other animals in the group.

In both welfare and practical terms, the most significant problem with exteriorized transducers is complications at the skin-implant interface. Ingress of infection is quite common, as is erosion or loosening of the skin-implant junction. It may be necessary to administer antibiotics to prevent or treat infection around skin buttons. Frequent use or continuous ambulatory monitoring will also increase the likelihood of irritation at the skin-implant interface.

It can be hard to avoid problems with skin buttons. Difficulties have been experienced with both shaved, clean skin and when hair growth has been allowed. The nature and degree of complications depends on the study species and the location at which the button interfaces with the animals' skin. For example, dogs have very loosely attached skin, especially in the region of the scruff of the neck, where skin buttons are commonly placed. There are fewer complications with species that have 'tighter' skin such as the domestic cow, and relatively fewer problems occur when buttons exit the skin overlying the skull in a range of species including guineapigs, domestic sheep and humans (e.g. Jarvik *et al*. 1998). Buttons should therefore be sited where skin is relatively less mobile wherever possible.

Ideally, skin buttons would be biocompatible so that animals' skin could adhere to them, and new materials such as titanium meshes are currently being researched and developed. The Working Group believes that total implants are thus currently to be preferred, and scope to achieve better tissue anchorage should be explored in full if cables or connectors are to be exteriorized.

Recommendations:

- **Use total implants rather than skin buttons or other exterior components where possible.**
- **If exteriorizing cables or connectors is unavoidable, give careful consideration to**

suitable exit sites and ways of improving tissue anchorage.

8 Basic principles of surgical implantation

Appropriate surgical skills and empathetic postoperative husbandry and care are absolutely essential if telemetry is to be conducted humanely. **The researcher and attending specialist veterinarian should work together and communicate effectively to ensure that all surgery is carried out competently and that pain is always adequately managed in all species, including rodents. Telemetry can in no way be considered a refinement unless this is achieved**.

The guidance below reflects current good practice; it is of course vital to ensure that everyone concerned with surgical procedures keeps up with new developments in surgery and pain prevention and management. The Working Group has produced a worked example of a surgical protocol that employs the principles set out in this Section, which can be downloaded at www.lal.org.uk/telemetry/.

8.1 Surgery—general considerations

The implantation of telemetry devices (which may be relatively large) requires considerable surgical expertise and dexterity. The ideal surgical technique should be minimally invasive, i.e. invasion of body cavities should be minimized to reduce the extent of surgical trauma, so that pain and discomfort are reduced as far as possible. Simplification of the procedure will also reduce operating times and make it easier to learn, both of which can benefit animal welfare.

The precise nature of each surgical procedure and whether it differs, however slightly, from established procedures should be given very careful thought. If the device body and probes have not been placed in the intended locations in the study species before, a pilot study should be undertaken in a small number of animals in case unpredictable complications occur. For example, the placing of probes in the same location can cause relatively few complications in rats but lead to substantial adverse effects, including death, in mice.

In most if not all cases, it will be in the best interests of the experimental animals and the project if surgery is performed by a team already possessing the necessary expertise in a particular implantation procedure. An in-house team, that would be on hand to deal with any post-surgical problems, is to be preferred wherever possible—over-reliance on one competent person is not desirable, in case they should become unavailable. These factors should always be considered before attempting a new surgical procedure.

Recommendations:

- **Always minimize invasiveness and simplify surgical technique as much as possible.**
- **Always conduct pilot studies for any new placement protocols, even if the same probe or device placements have been successfully used in other species.**
- **Consider setting up or using in-house surgical teams, or use appropriately certificated outside experts for implantation procedures.**

8.1.1 Expertise and training

The requirement for appropriate surgical training should not be underestimated, as this has a direct impact upon animal welfare. Training literature and videos from commercial companies should be used with caution, as quality can be variable, they may portray complex surgery that in reality requires comprehensive training, and they can also rapidly become dated as new techniques become available. Some people will never be physically competent to conduct the intricate surgical procedures that are frequently required and any responsible marketing strategy will recognize this. Advice and training in relevant surgical techniques must be obtained from veterinary surgeons and research scientists familiar with the devices and procedures being employed. A sound basic training in experimental surgery and good working knowledge of the devices are absolutely essential before progressing to implant insertions.

Telemetry surgery is best learned by direct observation of the procedure, followed by a period of assisting before finally performing the surgery under supervision. Video attachments that can display a small surgical field on a television monitor are very useful for both trainer and trainee. Written training records should be kept, to include duration of anaesthesia for each procedure (which should decrease with increasing competence); post-surgery observations such as food consumption, body mass and pain-coping behaviour; post-study pathology such as tissue adhesions, seroma or lead displacement; and technical failures due to poor device handling such as notches in cable casings. Periodic re-assessment of competence in procedures is strongly advised. Full consideration should be given to setting out benchmarks for surgeons and allocating resources to assessing them, which could be a function of local committees such as the UK ERP or US IACUC.

Artificial training aids should be used in the first instance wherever possible. Examples are artificial skin for suturing or tissues with veins for blood sampling or administering injections (e.g. Bell Isolation Systems Ltd, Appendix 1) or the Microsurgical Developments PVC rat model (Braintree Scientific, Inc., Appendix 1). The Group is not aware of any training aids that simulate fine blood vessels for cannulation at the time of writing, but new training aids are constantly being developed and so the potential for using artificial systems should be continually reviewed. Dummy telemetry devices should also be made available during training, so that users can become familiar with the careful handling techniques that are required. Most telemetry companies will supply these on request.

Recommendations:

- **Ensure that nobody carries out surgical procedures to implant devices unless they are highly skilled and appropriately trained, with complete working knowledge of the devices.**
- **Remember that, like animal tissue, telemetric devices are fragile and easily damaged—breaking a device during surgery could have a direct impact on welfare, for example by extending surgery time.**
- **Plan studies to allow for training time—surgery should not go ahead unless everyone involved is competent.**
- **Keep written training records and review them periodically.**
- **For attending veterinarians: monitor each surgeon's success rates and the incidence and nature of complications.**
- **Do not rely solely on material produced by commercial companies—seek additional advice and training aids.**
- **Replace animals with artificial training aids wherever possible.**

8.1.2 The use of animals to gain manual skills

In the UK it is permissible to use terminally anaesthetized animals during the development of novel biotelemetry techniques. However, the use of animals to gain manual skills to apply existing techniques, before going on to conduct regulated procedures, is *not* justified and the Working Group concurs with this view. The necessary skills can be developed initially in *ex vivo* training systems and then further developed under supervision during the course of experimental procedures.

In countries where the use of animals to develop manual skills in surgery is permitted, this training should only be performed in terminally anaesthetized animals. Each establishment should exercise careful control over the use of animals in such programmes to ensure that:

- their use is necessary and justifiable;
- there is a demonstrable benefit, i.e. the complication rate is lower and the success rate higher for operators who have had *in vivo* training (NB: this would not in itself justify *in vivo* training, but would indicate a need to improve on alternative training methods);
- the trainees have been provided with suitable training before embarking on live animal work;
- animals designated for terminal training procedures are treated with respect and

provided with good-quality housing and care; and
- terminal anaesthesia is competently administered and monitored.

Recommendations:
- **Question the justification and necessity for using living animals to develop manual surgical skills.**
- **If the use of living animals to develop manual skills is permitted, stringently control their care and use and ensure that they are only used under terminal general anaesthesia.**
- **Continually monitor and review operator success rates following *in vivo* and alternative training techniques, with the aim to replace living animals.**

8.1.3 Asepsis

Strict aseptic technique is essential where chronic implantations of foreign objects are being performed. Most infections originate from the skin, so special care needs to be taken when sterilizing implants and the skin at the operation site. Before anaesthesia for surgery, animals should be examined for the presence of any intercurrent infections (e.g. skin infections or bite wounds) which will increase the risk of implant infection, even if they are remote from the surgery site. Animals with intercurrent infections should not usually be subjected to implantation surgery in laboratory conditions, although this may be unavoidable in the field (see Section 11.1).

Broad-spectrum prophylactic antibiotics are justified for extensive surgery and large or complex implants in certain species. Infections usually occur within the first 8 h following surgery, so antibiotic administration should take place before surgery begins. It is essential to choose an appropriate agent in relation to its activity and unwanted side-effects in the species in question, taking into account the practicalities of administration. For example, it may be appropriate to administer an initial dose of an easily absorbed, short-term antibiotic (e.g. in malt loaf or banana bread for primates) followed by a longer acting agent. Antibiotic use should always be discussed with a veterinary surgeon when planning such surgical procedures.

Recommendations:
- **Provide and maintain high standards of surgical facility.**
- **Administer prophylactic antibiotics before surgery, e.g. intravenous soluble antibiotics immediately after induction. Discuss the use of prophylactic antibiotics with your attending veterinarian.**
- **Always maintain strict aseptic technique and ensure that implants have been appropriately sterilized and do not leak.**
- **Check animals carefully for wounds and infections before operating.**

8.1.4 Fitting implants, cables and catheters

Tissue pockets dissected to contain implants should be large enough to contain the device without undue tension; yet not too large, as this predisposes to seroma, haematoma and migration of the implant. Devices should always be sutured to muscle fascia (not tied to muscle fibres) using inert, non-absorbable sutures (e.g. Nurolon™, Ethicon); suture holes or tabs may be incorporated into the construction. Polyester fabrics (mesh or velour) may be glued to implants to facilitate anchorage by sutures to provide short-term holding, then ingrowth of fibrous tissue to provide longer-term anchorage. The use of absorbable sutures is not recommended, as implants may move or migrate after degradation of the material has occurred.

Cables and catheters require very careful handling because their silicone casings are 'notch sensitive', i.e. any small nicks in the outer layer will propagate inward and ultimately allow ingress of fluid into the electrical components of the device. The use of metal instruments on them should therefore be minimized. Cables and catheters also require careful routing to protect them from stresses and strains that could result in fatigue fracture or kinking. They should not be placed under any tension, make sharp bends or be subjected to repeated movement. Note that tunnelling cables under and out of the skin during surgery can compromise asepsis, especially where animals are turned over. Tunnelling should therefore be avoided or conducted with great care.

It is generally undesirable to anchor cables except at points of attachment, i.e. transducer attachment sites and attachment to implanted electronic devices or connectors. Where attachments have to be held in position in juvenile animals, sufficient slack may have to be left to allow for growth. For example, ECG signals can be weakened and even lost, or cannulae inserted into blood vessels may pull out due to differential growth. It is important to note that tissue may adhere to catheters and biopotential leads, restricting any 'slack' allowed for growth in young animals.

Anchoring cables by use of encircling sutures and ligatures is not recommended, due to the risk of abrasion of the insulating coat by the material. Instead, suture tabs should be glued to cables of catheters where it is necessary to place anchoring sutures. Porous polyester cuffs (e.g. Dacron™ Velour) may also be glued to cables or catheters to permit long-term anchorage by ingrowth of fibrous tissue. Porous cuffs can also be placed just distal to the skin-implant interface of an exteriorized cable to provide physical anchorage and a barrier to the ingress of infection from the skin surface.

Recommendations:

- **Site large implants in a body cavity or deep in a layer of muscle or fat where possible, to prevent necrosis of the overlying skin.**
- **Handle cables and catheters very carefully and consider where they will be sited in relation to an animal's behaviour when conscious—avoid areas of repeated extensive movement or areas that will be stretched by growth.**
- **Research growth rates and patterns carefully and devise an attachment protocol to reflect this.**
- **Avoid tunnelling where possible, and ensure as far as possible that asepsis is not compromised.**
- **Do not anchor cables apart from points of attachment.**
- **Use a suitable, biocompatible non-absorbable suture for anchoring; use monofilament polypropylene (e.g. Prolene™ Ethicon for blood vessels).**

8.1.5 Inserting transducers into blood vessels

Inserting pressure transducers into blood vessels or cardiac chambers can be difficult and demanding. Care must be taken to ensure that the intravascular portion of the device remains free from contamination. The use of non-linting swabs and surgical sponges is strongly recommended and powdered surgical gloves should not be worn, because lint or glove powder can easily block fine blood vessels such as the rat aorta or vessels branching from it. Where cyanoacrylate tissue adhesives are used to anchor transducers into vessels or seal the insertion site, transducers must not be advanced while the adhesive is curing as this can create marked thrombosis. Only medical grade tissue adhesives should be used (e.g. VetBond™, 3M) as industrial type adhesives frequently contain toxic materials. Minimal amounts of tissue adhesive should be used as excessive amounts of cyanoacrylate have been implicated in the induction of tumours (fibrosarcoma) (Matsumoto & Heisterkamp 1969). Care should also be taken to avoid contact of adventitial tissue with the intima or lumen of the artery, as this is highly thrombogenic.

Recommendations:

- **Take the utmost care to ensure that transducers placed into vessels are completely free from contamination such as adhesive, lint or glove powder.**
- **Do not use powdered gloves.**
- **Use only minimal amounts of medical grade adhesive.**
- **Never attempt to insert transducer heads into the lumen of the thoracic aorta unless you have extensive expertise in thoracic and vascular surgery.**

8.1.6 Checking and closing

Checking implant function should, wherever possible, be done at each step of the implantation procedures and always before the animal is taken from the operating table to begin recovery. Ideally this checking should be done before wound closure is commenced and then again on completion. Signal strength and device function should be optimized at the time of surgery wherever possible (some transducer types require a period of tissue ingrowth to achieve correct function).

Closure of surgical wounds around implants should eliminate as much dead-space as possible. It is highly undesirable to have a single layer of skin closure over an implant and there should be at least one additional layer of closure deep to the skin to ensure that there is no direct contact between a healing skin incision and a foreign body implant. Refinements in suturing techniques enable animals to be regrouped very quickly after surgery, e.g. after 24 h, so it is essential to ensure that those responsible for wound closure are adequately trained. See also Part B for guidance on regrouping animals following surgery.

Recommendations:
- **Check implant function before wound closure is commenced and before recovery wherever possible.**
- **Never have just a single layer of skin closure over an implant.**
- **Avoid incisions over the site of a bulky implant.**
- **Research suturing refinements and ensure that they are employed.**

8.1.7 Standard Operating Procedures

In some cases, for example where data from studies will form part of formal regulatory submissions, work must be done to auditable high standards (e.g. Good Laboratory Practice, GLP). Whether or not this is a requirement, it is advisable to consider a quality system for work involving telemetry studies with documented benchmarks and Standard Operating Procedures (SOPs). This can be invaluable when troubleshooting failed or problematic studies. Consideration should be given to accuracy in calibration, data recording and checking, noting the serial numbers of devices and so forth. SOPs should contain sufficient critical detail to ensure that surgical procedures are consistent between animals and that the correct transducer placement has been ensured and documented during surgery.

Recommendations:
- **Consider introducing an appropriate quality system for studies with documented SOPs.**
- **Document and regularly review failure rates for benchmarking.**

8.2 Anaesthesia

Appropriate methods of anaesthesia and expertise in their use are essential for telemetry surgery. Key questions that need to be considered when choosing an anaesthetic agent include (see also Flecknell 1996, pp 70–73):

- Will it provide an adequate depth of anaesthesia for the procedure?
- Is it especially aversive to the study species or strain?
- How can it be delivered so as to minimize distress?
- What will the physiological impact be?
- How long will the recovery time be (especially for field studies involving release)?
- Is it compatible with the objectives of the study?

Advice and assistance on the most appropriate method of anaesthesia in each case should be obtained from an experienced, specialist veterinary surgeon and regular literature searches are absolutely essential. The questions set out above are addressed in a number of publications including those in the list at the end of this section, and so they will not be expanded upon here. The Working Party would, however, emphasize the following points:

Minimizing any distress caused by anaesthesia

All anaesthetic agents are likely to be aversive to animals, especially at high concentrations. The potential for distress must be minimized by researching which is least likely to be aversive for a given strain and ensuring that it is delivered at an appropriate rate (taking into account all other relevant factors including those listed above). For example, carbon dioxide is highly aversive for BALB/c mice and Wistar rats (and has been shown to be aversive in all species studied), whereas halothane is less aversive than isoflurane for both strains, and BALB/c mice tolerate enflurane equally well (Leach *et al*. 2002).

Compatibility with study objectives
Low solubility, volatile anaesthetics such as isoflurane are the agents of choice for telemetry studies because they permit effective control of depth of anaesthesia, are rapidly eliminated and are not (or only minimally) metabolized. In most laboratory projects, there will be adequate time to allow full recovery from effects of anaesthesia and elimination of drugs and their metabolites. For short-term projects or those involving the release of wild animals, however, it will be necessary to ensure that anaesthetic agents have minimal lasting effects.

If there is a genuine (non-economic) reason not to use isoflurane, agents that can be adequately and permanently reversed through the use of antagonists are recommended. However, nearly all general anaesthetic agents have some residual effect for several days and this has to be recognized and taken into account (see Wadham 1996). This is particularly important for free roaming or wild animals, permitting early and safe release, but they may have to be monitored in some form of extensive captivity before they are completely released to the wild.

Recommendations:

- **Ensure that anaesthesia protocols are up to date, reflect good practice and are regularly reviewed.**
- **Ensure that all animal welfare and scientific considerations have been taken fully into account when choosing anaesthetic agents.**

The Working Group recommends the following standard texts on anaesthesia:

Flecknell, PA (1996) *Laboratory Animal Anaesthesia*, 2nd edn. London: Harcourt Brace & Company

Gleed RD, Ludders JW (eds) (2001) *Recent Advances in Veterinary Anesthesia and Analgesia: Companion Animals*. International Veterinary Information Service: **http://www.ivis.org/advances/Anesthesia_Gleed/toc.asp**

Kohn DF, Wilson SK, White WJ, Benson GJ (1997) *Anaesthesia and Analgesia in Laboratory Animals*. New York: Academic Press

Seymour C, Gleed R (eds) (1999) *Small Animal Anaesthesia and Analgesia*. Cheltenham, UK: British Small Animal Veterinary Association

8.3 Pain management

Surgical procedures cause animals discomfort and pain, even with appropriate analgesia. Pain causes suffering and distress, slows recovery, can reduce food and water consumption, interferes with respiration and can slow healing (Flecknell 2000). **The provision of appropriate pain relief following all surgical procedures on all species is therefore absolutely essential**. Despite this, analgesia is still sometimes not provided following surgery. Reasons for this and current thinking on pain management are summarized in Table 3 (simplified from Flecknell & Waterman-Pearson 2000; see also Soulsby & Morton 2001, Roughan & Flecknell 2002).

Post-surgical pain also affects a wide variety of physiological parameters in an unpredictable manner, which may have a significant impact on the validity of any experimental results. For example, respiratory function may be impaired by restricted breathing if there is thoracic pain, or by hyperventilation due to non-thoracic pain. Skeletal pain can restrict mobility, thus reducing food and water intake and depress appetite *per se*.

In the context of implanting telemetry devices, pain can be divided into three main stages:

- Pain during surgery—even with appropriate anaesthesia, surgical pain can alter neurones in the central nervous system such that the injured site and adjacent sites become more sensitive following recovery (hyperalgesia) and even non-painful stimuli can become painful (allodynia) (Livingston & Chambers 2000). This central sensitization (or

Table 3 Current thinking on post-surgical analgesia for animals

Historical reasons for withholding analgesia	Current thinking
Pain has a protective function—if it is relieved, animals will become too active and damage incision sites	Analgesics rarely completely relieve pain—sufficient protective function will remain to prevent damage. Alleviating pain will speed recovery of normal physiological functions
Analgesics have side effects that may be undesirable	Side effects can almost always be avoided or managed by choosing appropriate agents and doses or by temporarily modifying husbandry protocols*
There is a lack of guidance on safe doses	More information is now available on a range of agents and doses, due to increasing concern about pain in animals

*See Roughan & Flecknell (2002) for examples

'wind-up') must be prevented by administering analgesia *before any incisions are made* as well as post-surgery (Dobromylskyj *et al.* 2000; see below).

- Over the next few days following surgery, the body normally mounts an inflammatory response which can be painful due to the release of local tissue substances such as prostaglandins. The pain management protocol at this stage should therefore include anti-inflammatory drugs.
- Pathological changes occasionally occur that could cause discomfort or pain e.g. chronic inflammation, chronic low-grade infection, neuroma, keloids, wound breakdown, pressure sores or capsule formation. The ability to recognize behavioural and physiological changes that indicate the presence of such pathologies is essential, as is a protocol to deal with chronic discomfort and pain.

8.3.1 Analgesia

It is absolutely essential for the attending veterinarian to keep up with developments in pain management, regarding both the production of new agents and current thinking on the most effective way to use all agents. Two especially important factors in acute pain control are the timing of analgesic administration and the way in which different classes of analgesics are combined (Dobromylskyj *et al.* 2000). Chronic pain may well be more difficult to alleviate and the agents, dosing protocols and therapies employed will need to be carefully thought out and implemented (see Brearley & Brearley 2000).

Timing—pre-emptive analgesia

Post-surgical pain can be largely prevented by administering pre-emptive analgesia before surgery begins, in conjunction with post-operative top-ups. If this protocol is not followed, established pain can only be controlled, which is more difficult to achieve (Dobromylskyj *et al.* 2000). It is very important to match the level of medication with the degree of surgical invasiveness. It is also essential to appreciate that additional medication will still be required postoperatively. Pre-emptive analgesia can also result in a reduction in the dose of anaesthetic drugs required, reducing the risk to the animal (see Dobromylskyj *et al.* 2000).

Using different analgesics—multimodal pain therapy

The clinical pain experienced by an animal involves many different pathways, mechanisms and transmitter systems, and so the use of a single class of analgesic is often not sufficient to control pain. Multimodal pain therapy, using two or more different agents that act on different parts of the pain system, is now known to relieve discomfort and pain far more effectively. Another benefit of this approach is that it helps to overcome problems associated with differing speeds of action of different agents (Dobromylskyj *et al.* 2000).

For example, an opioid (e.g. buprenorphine) and a non-steroidal anti-inflammatory drug

(NSAID) are often used in combination to reduce post-surgical pain to an extent that would not be possible using either drug alone. Opioids act by limiting the input of nociceptive information into the central nervous system (CNS), thereby reducing central hypersensitivity, whereas NSAIDs act peripherally to decrease inflammation, limiting the nociceptive information entering the CNS. In addition, NSAIDs act centrally to limit central changes induced by nociceptive information that does get through. For further information and examples of perioperative analgesic protocols, see Dobromylskyj *et al*. (2000) and the example materials and methods section at www.lal.org.uk/telemetry/.

Chronic pain

If chronic discomfort or pain occurs, it will be necessary to decide whether it should be alleviated by administering analgesia, operating to repair poor healing (paying due and full regard to ethical and legal constraints) or killing the animal. In an experimental situation, euthanasia is likely to be the most realistic option on both scientific and ethical grounds. If it is considered justified to provide analgesia so that the animal can remain alive with reduced pain or discomfort, veterinary advice and close supervision are essential (see Brearley & Brearley 2000). If and when animals are killed, necropsy results should be communicated to the surgical team and any pain-coping behaviours seen during life should be correlated with gross and histological observations *postmortem* so that improvements in training and pain management can be made as appropriate.

Recommendations:

- **For attending veterinarians: ensure that you have access to all the resources that you need to keep up with developments in pain management.**
- **Provide pre-emptive analgesia for all animals undergoing surgery.**
- **Use more than one class of analgesic agent to act on different points on the pain pathway.**
- **Match the doses and duration of action of analgesics to the degree of surgical invasiveness.**
- **Make sure that a protocol for dealing with chronic discomfort and pain is in place before projects begin.**
- **If wound healing is poor, communicate necropsy results to the surgical team so that it can act on them.**

The Working Group recommends the following texts on pain management:

Flecknell PA, Waterman-Pearson A (eds) (2000) *Pain Management in Animals*. London: WB Saunders

Gleed RD, Ludders JW (eds) (2001) *Recent Advances in Veterinary Anesthesia and Analgesia: Companion Animals*. International Veterinary Information Service: **http://www.ivis.org/advances/Anesthesia_Gleed/toc.asp**

Hawkins P, *et al*. (2001) Laboratory birds: refinements in husbandry and procedures. *Laboratory Animals* **35**(Suppl. 1), 1–163

Hellebrekers L (ed) (2000) *Animal Pain*. Utrecht, Netherlands: Van Der Wees

Mathews KA (2000) Management of pain. *Veterinary Clinics of North America, Small Animal Practice* **30**, July

Tranquilli WJ, Grimm KA, Lamont L (2000) *Pain Management for the Small Animal Practitioner*. Jackson, Wyoming: Teton New Media

8.3.2 Postoperative husbandry and care

Tender Loving Care (TLC), i.e. good nursing, helps to speed recovery and to minimize the impact of surgical procedures on animals. Attention to helping the animal return to normal feed and water intake by offering treats appropriate to the species such as fruit, vegetables or jelly and so on, as well as the normal diet in an appropriate form, is very important (Baumans *et al*. 2001; example at www.lal.org.uk/telemetry/). Animals well socialized with humans may appreciate extra contact from favourite carers after surgery, and this should be allowed for.

A good-quality environment should always be provided for animals, but is likely to play an especially important role in helping to shift their attention from any discomfort, pain or distress that procedures may have caused them (e.g. Gentle 2001). Serious consideration should be given to providing a stimulating but comfortable environment for animals following surgery, while ensuring that animals can also be monitored effectively. Social stimulation is important and so social animals should be kept in compatible groups both before and after implantation unless there is a good veterinary reason for not doing so (see Part B, Hawkins *et al.* 2004). Animals with external devices may attract attention from cage or pen mates and the device may have to be protected (this is not a problem if wholly internal devices are used).

Recommendations:

- **Think (from the animal's point of view) about what is necessary to provide a comfortable and comforting environment to speed recovery and how you can provide this.**
- **Provide sufficient environmental and social stimulation to shift attention away from any discomfort and pain, but ensure that animals are not subjected to unnecessary risk and that they can be effectively monitored.**

8.4 Monitoring animals following surgery

The importance of an effective system for recognizing and assessing discomfort, pain or distress cannot be over-emphasized. The health and well-being of all animals with implants should be assessed at least twice daily, and any deviations from normal body weight, body temperature, appetite, feeding behaviour, gait and faecal quality, should initiate a full veterinary examination. Regular clinical examination should also be performed by a veterinarian, as appropriate to the extent of the implant surgery and intensity of experimental work. For example, at one group member's establishment, rats have a full clinical examination daily following suture removal, weekly for the first month, then monthly thereafter.

A team approach to pain management, involving all those concerned with the care and use of animals in a particular project and the relevant committees, is highly recommended (Morton & Griffiths 1985, Morton 2000). The team should decide which criteria are to be used for assessing animals, how observations will be recorded and reviewed, and what course of action should be taken if there are welfare or health concerns about an animal (see sample score sheet with box for free text, Appendix 2).

Observation records should be kept (e.g. for 5 years) and regularly reviewed to assess the effectiveness of surgical technique, analgesia regimens, postoperative care and housing and husbandry protocols. For more information on current techniques used for pain assessment in the UK including downloadable score sheets that can be adapted to specific procedures, see Hawkins (2002).

One advantage of implanting telemetry transducers designed to transmit physiological data is that they can be used to monitor the effectiveness of postoperative care. Variables such as heart rate, body temperature, and the activity of an animal will normally have a circadian rhythm and the time taken for return to normal rhythms could reflect the impact of the surgical procedure, anaesthetic, analgesic and postoperative care protocol etc. (Lawson *et al.* 2001) even though it is not currently possible to know what the 'normal' levels were for these variables before surgery. The length of time that elapses before circadian rhythms are reinstated is also a useful measure of postoperative recovery and could be used to compare different analgesics, for example (Ambrose 1999).

There are a number of objective techniques for assessing pain or distress (see Hawkins *et al.* 2002) and these should be researched and their potential application considered for each project. Examples of these assessment methods include video analysis of postoperative behaviour (Roughan & Flecknell 2001), gait analysis (Clarke & Still 1999) and non-invasive body temperature monitoring (in Hawkins *et al.* 2002).

Recommendations:

- **Monitor animal health and well-being at least twice daily following surgery, using score sheets with boxes for free text.**
- **Make sure that the pain management team is communicating well and has set up an effective protocol for regular reappraisal.**

- **Ensure that clinical examination by a veterinarian takes place at appropriate intervals.**
- **Use telemetered variables to monitor well-being and help to define best practice.**
- **Research new techniques for recognizing pain and distress; apply them wherever they can be used to refine procedures and postoperative care.**

8.5 Potential postoperative complications and repairing surgery

Beyond the likely intraoperative risks of surgical procedures covered elsewhere in the literature (fluid loss, heat loss, pain from extensive surgical manipulations) and general risks associated with any surgery (for example the animal removing sutures) there are a number of postoperative risks that are specific to telemetry.

Tissue damage—the degree of risk depends on the surgical approach, so a number of approaches should be considered if possible. It is important to research this thoroughly and to consult with colleagues, as less invasive approaches do not necessarily reduce postoperative pain (K. Kramer, personal communication). Tissue damage may be due to inexperience, e.g. a novice surgeon may take too long to implant into the descending aorta once it is occluded. In this instance better training, more practice and use of 100% oxygen in the anaesthetic should reduce the risk.

Infection—when implants are in place it requires far fewer bacteria to cause clinical infections compared with clinical surgery. Infections around implants are extremely difficult to clear if a capsule has formed, even with high-dose antibiotics for a number of days, due to reduced penetration of drugs. Experience suggests that remission can be obtained for a sufficient period to allow an animal to be used on study, but clinical signs usually recur in a matter of weeks.

Adhesions—chronic low-grade inflammatory lesions may form in association with implants, causing chronic discomfort or ill health. Note that following extensive cardiothoracic instrumentation in the dog there will be widespread adhesions inside the chest. This may result in altered appearances of the thorax on radiographs or ultrasound investigations and it is possible to hear a range of adventitious sounds associated with rubbing of silicone coated cables (squeaking). These are generally normal features of instrumented dogs that the veterinary clinician should bear in mind.

Wound breakdown—there is a risk of wound breakdown associated with any surgical procedure, but when an implant exerts pressure on the overlying suture line this risk is greatly increased. Placing the suture line away from the implant can reduce this risk, but can make the surgery more challenging by requiring working in deep tissue pockets (see seroma below). If skin erosions associated with pressure exerted on the skin by subcutaneous implants do occur it may be possible to attempt repair surgery, but this is rarely more than palliative to ensure that a study can be completed.

Seroma—with extensive subcutaneous dissection and tunnelling, seromas frequently develop in the postoperative period. The risk can be reduced in several ways including minimal dissection (but see wound breakdown), subcutaneous sutures to reduce dead space, firm anchoring of implants, restrictive bandaging if possible (e.g. not for inguinal implants in male dogs). Drains are not appropriate due to the risk of entry of bacteria, but aseptic drainage can be performed if a seroma grows to the extent that an animal becomes uncomfortable.

Implant or battery failure—many telemetry devices can be easily damaged. All should be checked for functioning pre-surgery, but if there is any risk of intraoperative damage then the implant should be checked once in place and before the wound is closed. A spare, sterilized implant should be on hand to replace the damaged one. Postoperative implant failure presents significant legal and ethical issues that must be addressed before repeat major surgery can be undertaken. If a battery fails part of the way through a lengthy study and replacing it could enable an animal to return to the study, then this may be ethically preferable to implanting another animal (but note that recalibration may be necessary; see below).

Surgical repairs—judgement on whether animals should be operated on again will have to be undertaken on a case-by-case basis and it is, of course, essential to consult with the attending veterinarian and relevant animal care and use committees. Advice must also be obtained from whichever body implements the national law regulating animal experimentation (e.g. the Home Office Inspectorate in the UK).

The invasiveness of the surgery required to do this is an important factor; minor subcutaneous surgery where any pain is well controlled may be acceptable, whereas more substantial surgery (e.g. re-entering a body cavity) may not be. If fibrosis associated with chronic implants would make it difficult to repeat the same surgical approach, then for all but the simplest devices a different surgical site should be chosen. In most cases such repeat surgery cannot be justified.

If complications occur during repair surgery, the animal should be killed immediately and without regaining consciousness. The need to avoid serious suffering should be given top priority at all times.

Recommendations:

- **Be aware of all the potential complications set out in this section—think about how you could try to prevent them in your project and how you would address them if they occurred.**
- **Ensure that the ethical and legal implications of repair surgery have been considered in full (i.e. when weighing the harms and benefits) and that due regard is paid to ensuring the welfare of an individual animal and preventing suffering.**

8.6 Long-term monitoring

The welfare and health (including haematology, blood biochemistry and growth rate where appropriate) of animals on long-term studies should be regularly reviewed by the attending veterinarian as part of a full clinical examination. Ongoing assessments should be conducted to monitor for behaviours indicating that animals are unable to cope with their environment, such as stereotypies. Such behaviours should be regarded as unacceptable and the situation addressed immediately if they occur, for example by obtaining expert advice (e.g. from an animal behaviour counsellor or experienced ethologist) on improving the animals' environment or providing more socialization with humans or other animals as appropriate. If animals are still unable to cope with their environment, they should be taken off the study. Husbandry and care for all animals should also be reviewed if stereotypic behaviour is observed in *any* animal. Besides the moral imperative to maximize animal welfare, it is the experience of Working Group members that animals are also easier to handle and work with (because they are less stressed) if adequate investment is made into environmental and social enrichment for them.

'Data mining', where experimental variables are used to monitor well-being and trends in physiological parameters, is recommended wherever possible. Ethograms and time-budgets should be compared before and after devices have been fitted; behaviour of wild-caught animals released into the field can be compared with conspecifics.

Recommendations:

- **Ensure that veterinarians and others responsible for animal care assess animals regularly.**
- **Prevent and alleviate stereotypies, for example by using appropriate environmental and social stimulation and by consulting experts.**
- **Use animal behaviour and experimental variables to monitor well-being.**

9 Re-use of animals

Animals used in telemetry studies are often subject to re-use (NB: legal constraints apply to re-use in some countries including the

UK[3]). There are scientific, ethical and welfare issues that must be considered when planning individual studies and in deciding how many procedures implanted animals ought to undergo. Animals with telemetry implants can provide extremely valuable scientific data and are also valuable with respect to the time and resources spent in training and preparing them. The surgery that these animals will have undergone involves a degree of suffering, even with best surgical and analgesic practice.

At the end of each study, the health and welfare of every animal should be reviewed and a decision made on whether or not s/he should be rehomed, killed or retained for possible further use. It is important that any request for re-using an animal is considered on its own merit, and that a balance is made on the cost to each established animal versus that to a naïve animal where this is relevant. A case for re-use may seem easy to justify where the initial project may have had a significant impact, as for example in a surgical preparation, and there is likely to be little additional harm to the individual animal, for example on a mild dosing study. However, it is important also to consider the impact of the housing and husbandry on the individual, e.g. whether the animal has become institutionalized, and any potential adverse effects of this on the scientific outcome. For animals maintained long term, it is essential that additional consideration is given to ensuring that the animals' behavioural, social and physiological needs are adequately addressed.

Where re-use is likely, subsequent procedures should be limited and rationalized, e.g. by restricting them to the administration of similar or related agents. It is necessary to ensure that there are no residual effects of previous treatments by setting a minimum recovery or wash-out period, and checking that relevant physiological parameters have returned to control levels. The experimental protocol may include a positive control substance and the magnitude of the response to this may be used to confirm that animals are eligible for re-use. A comprehensive clinical evaluation is also absolutely essential and a signed certificate confirming the health status of the animals should be completed by the attending veterinarian as a permanent record and ultimate authority for re-use.

The Working Group believes that limits must be set on the overall usage of an individual animal, and these may be defined by national regulators, ethics or animal care and use committees or veterinary staff (e.g. the Named Veterinary Surgeon in the UK). Decisions on re-use should involve consideration of the number of re-use scientific protocols, any adverse effects experienced in previous experiments and how well adjusted the individual is to the housing and husbandry systems. As this is very much an issue involving the judgement of professional individuals on a case-by-case basis, no numerical limits are offered.

Recommendations:

- **Make sure that all the ethical and welfare issues are fully addressed when making decisions about re-use, in addition to the scientific issues.**
- **Ensure that you are complying with the relevant legislation if animals are re-used.**
- **Always make sure that recovery and wash-out periods are adequate.**
- **Set up a system where authority for re-use depends on verifiable certification of health status.**
- **Consider *all* the potential welfare costs to each individual, including those associated with housing and husbandry, when making a decision about re-use or continued use.**

10 Removing implanted devices and rehoming or releasing

Recovering implants presents an opportunity for examining how well the implantation surgery was performed. For this reason, devices should be removed by a member of the surgical team in consultation with the attending veterinarian whenever possible and

[3]UK law permits the re-use of surgically prepared animals on a specified number of occasions provided that: (i) the animal has not suffered significant adverse effects; (ii) the scientific objectives of the subsequent study would not be compromised by any previous procedure (e.g. drug interactions); and (iii) an animal with the particular surgical preparation is necessary for the study.

the results communicated to the rest of the team so that any required improvements can be implemented. Devices should also be recalibrated at that time. If animals are to recover from removal surgery, very careful consideration of the ethical, legal and practical issues involved is essential.

Most animals are killed at the end of telemetry studies for scientific or humane reasons, but this should not be routinely done without fully exploring the potential for rehoming or release[4]. Animals are valuable in their own right as individuals and have a strong interest in remaining alive. Removing a device with recovery will inevitably cause suffering to a degree, but this is not a reason for routine euthanasia and each case should be judged on its own merits. It is possible that the benefits of years of good-quality life as a companion animal or the freedom to return to the wild, or a sanctuary, and possibly breed may outweigh the suffering associated with removal surgery in some circumstances. In such cases, it is the responsibility of the investigator to ensure that the animals are given the chance to enjoy those benefits and this should be addressed at the project planning stage.

As with repair surgery, the welfare implications of removing devices should be considered before this is undertaken as a recovery procedure. If an implant is very superficial, then removal may involve relatively little suffering for the animal. However in many cases the implant will be enclosed by a fibrous capsule that can be very thick, and it can be extremely difficult to distinguish landmarks such as blood vessels and nerves. Extensive dissection may be required, with implications for pain and distress in the recovery period as well as delayed healing. If animals are to be rehomed under close supervision, it may be preferable to leave devices in place.

Rehoming animals as companions (e.g. dogs) or in collections of animals (e.g. primates, birds) is, in general, preferable to release in the field, because of the increased potential for monitoring well-being, and providing veterinary treatment and euthanasia if this should be necessary. Release may be a humane option (for example) where animals have been captured as adults, held for short periods, are in good health and have not learned any behaviours that would disadvantage them in the field. For both rehoming and release, the future quality and quantity of life that animals may experience should be weighed against the likelihood of them suffering because they have been used in research (see LAVA 2001). It is most important also to be certain that released animals do not carry infectious agents that may be imported to the wild with them (Woodford 2001), and that their release will not compromise the welfare of the existing wild population in other ways (Woodford & Rossiter 1993, Kirkwood 2000). Expert advice from the attending veterinarian and bodies such as the IUCN Veterinary Specialist Group or the US Fish and Wildlife Service will be necessary and there may be legal considerations, e.g. in the UK release has to be authorized by the Project Licence.

Recommendations:

- **Do not routinely kill animals without fully exploring the potential for rehoming or release.**
- **Use device removal (with or without recovery) as an opportunity to monitor surgical standards; communicate results to the research team.**
- **If animals are to be released, obtain expert advice from the attending veterinarian and all other relevant bodies; ensure that all necessary legal permission has been obtained.**

11 Telemetry studies in the field or using wild animals

There are three key issues associated with studies on wild animals that raise particular ethical and welfare concerns:

(1) Capture and handling by humans (who are predators) will inevitably cause distress to wild animals. While many domestic animals find handling by humans stressful,

[4]Note that if an animal with a surgical implant is euthanized and the body incinerated, there is a risk of explosion if the implant is left *in situ*—if in any doubt the device should be removed prior to incineration.

this is likely to be greatly increased in wild animals who are not habituated to humans and not accustomed to a predictable routine. Restrained wild animals may lie very still and appear not to be stressed, but this behaviour, tonic immobility, should not be misinterpreted as them not experiencing stress in some way. Objective physiological measurements indicate that animals who are apparently coping well with being handled can be experiencing distress (Culik *et al*. 1990); in the case of animals undergoing invasive research such distress will be compounded by surgical procedures.

(2) The physiological impact of telemetry devices, whether attached externally or implanted, can have far more serious implications for wild animals in the field than for laboratory animals. For example, the consequences of a reduction in the ability to forage or of increased grooming time may not be significant in laboratory animals but could be severely debilitating or fatal for free-ranging wild animals. The physiological impact of devices on animals can be divided into covert effects, such as elevated metabolic costs of transport, and overt effects, some of which are set out in Table 4 (see Section 7, Kenward 2001).

(3) There is often little potential for monitoring wild animals following their release (see below). Animals in the field could suffer through their inability to feed, thermoregulate or defend themselves if humans are not in a position to intervene.

Imposing a physiological burden on an animal who will subsequently be released and have to survive and function in the field should therefore never be undertaken without strong scientific justification. Any proposed project that involves catching[5] or using wild animals should be subject to comprehensive ethical review by the appropriate committees (cf. Kenward 2001, see also guidance for ethics and animal care and use committees at www.lal.org.uk/telemetry/). If a project is deemed to be justified, all procedures should be fully refined *and* the potential for devices and procedures to have a significant impact on behaviour and scientific data should be fully researched and taken into account when making decisions on ethical and scientific acceptability (Culik & Wilson 1991, Vaughan & Morgan 1992, Wilson & Culik 1992, Kenward 2001).

Key procedures and events that need to be refined are set out in Table 5 (see also Table 1 on harms that apply to both wild and laboratory animals). Note that both covert and overt effects represent welfare costs to the animal that must be addressed and minimized, regardless of whether they have a

[5]Animals should never be removed from the wild for scientific purposes unless it is impossible to obtain them from commercial breeders.

Table 4 Examples of overt adverse effects of telemetry devices on wild animals (summarized from Kenward 2001)

	Potentially fatal consequences	Impairment of normal function
Short term	• Capture shock, leading to chilling and/or predation • Desertion of eggs, rejection of young **Be aware of, and avoid, high risk periods**	• Temporary reduction in foraging • Increase in preening or grooming at the expense of other behaviour **Revise device design** **Reduce handling time; consider costs and benefits of sedation**
Long term	• Fatal complications from implants • Tangling in harnesses • Attracting predators **Ensure that internal and external attachment protocols are fully refined**	• Chafing or cutting skin; feather loss • Impairment of movement, drag • Decreased foraging performance • Reduced tendency to move **Revise attachment protocol, device design and location**

Bullet points denote overt adverse effects; actions to prevent or alleviate them are in bold

Table 5 Potential adverse effects (i.e. sources of discomfort, pain, suffering and distress) especially associated with telemetry of wild animals

- Psychological stress due to human interference with habitat (e.g. studies involving recording vocalizations, video monitoring, removal of faeces)
- Possibly higher levels of stress and distress due to unfamiliarity with humans
- Capture
- Handling
- Restraint
- Confinement
- Transport
- Injury (including tagging and ringing)
- Marking (including altered behaviour of conspecifics towards animal)
- Recovery from sedation or anaesthesia
- Disruption of colonies of social species—those under study and others
- Increased risk of predation
- Reduced ability to catch prey
- Potential to lose condition while in captivity

significant effect on data quality or appear to be causing the animal a long-term problem. See Kenward (2001) for further guidance on detecting adverse effects.

As a further consideration, individual wild animals are part of communities and ecosystems that must necessarily be disrupted to a degree when individuals are trapped and removed (Gaunt & Oring 1999). The impact on, for example, other members of the captured animals' colony, other species and the environment are an essential part of the harm–benefit assessment and should be fully taken into account by relevant committees and decision-makers when assessing potential projects.

Finally, it is essential to obtain guidance from a statistician with respect to the minimum number of animals required and to make as realistic a judgement as possible, using all the information and advice available, on whether it will be possible to catch (and recapture, where appropriate) that number (Festing *et al*. 2002). If there is significant doubt about this, the project should not go ahead (see Kenward 2001).

Recommendations:

- **Ensure that any proposed project involving wild animals is asking a relevant and important biological question and has been subjected to comprehensive ethical review; also give full consideration to practical issues such as the ability to catch sufficient animals.**
- **If you have not already done so, read other relevant sections of the present report, particularly Sections 7 (selecting or designing a device) and 8 (surgery).**
- **Recognize that wild animals are liable to find capture and handling extremely stressful and that this represents an experimental 'harm'.**
- **Consider the additional harms that may be caused to other animals, other species and the environment by your project, and how they could be minimized.**
- **Test for and evaluate covert and overt adverse effects as far as possible; revise your protocols accordingly and communicate your findings.**
- **Fully and continually explore the potential for refinement.**

11.1 Surgical facilities at field research stations

Surgical standards in the field should follow similar principles to those in a laboratory operating theatre with the aim of avoiding sepsis and other causes of wound breakdown and of managing pain effectively—for guidance on all of this, refer to Section 8. Surgery on all species must be carried out using appropriate anaesthetics, suitable site preparation, aseptic technique, good surgical technique, adequate and timely analgesia, and wound care procedures that are suitable for the age and species being used. Access to adequate supplies of drugs, disinfectants and sterile instruments is essential and at least one assistant is necessary to monitor anaesthesia. If all of these conditions cannot be met, surgery in the field should not be contemplated. Any minor wounds already present should also be treated wherever possible to minimize the risk of their subsequent worsening, for example through infection, post-release.

Wild animals may appear to be resilient but this may be an adaptation to hide signs of pain or distress rather than a reflection of their true physical and psychological fitness or their resistance to infection. Specialist veterinary advice should therefore be sought regarding both analgesia and antibiotic regimens and appropriate programmes should be carefully planned. Prophylactic antibiotics can reduce the risk of infection in free-ranging animals and should be administered wherever necessary. For example, free-ranging animals can be given long-acting antibiotic preparations that last for 3 or 4 days. Less is known about suitable analgesic regimens for wild animals, however; opioids may be sedatives, and little is known about potential adverse effects of NSAIDs. It is also good practice to consult zoos or other organizations concerned with keeping wild animals regarding antibiotics and analgesics for particular wild species. Useful starting points on the internet are the International Veterinary Information Service (http://www.ivis.org/), WildPro (http://www.wildlifeinformation.org/) and the Electronic Zoo (http://netvet.wustl.edu/e-zoo.htm). For African animals, see the Wildlife Decision Support Services Capture and Care Manual (http://www.wildlifedecisionsupport.com/captureandcare/).

Every attempt should be made to contact scientists or veterinarians who have conducted implantation or other surgery on the species, to benefit from their experience. Furthermore, all surgical, anaesthetic, analgesic and antibiotic regimens should be correlated with available information about post-release morbidity and mortality rates and disseminated to others in the field (e.g. see Mulcahy & Esler 1999). It is part of the responsibility of the researcher towards experimental animals to evaluate and communicate any information related to refinement. There are a number of forums to facilitate this, e.g. the Forum on Wildlife Telemetry (http://www.npwrc.usgs.gov/resource/tools/telemtry/telemtry.htm).

Recommendations:

- **Do not operate on animals in the field unless you can provide surgical standards equivalent to those that would be expected in the laboratory.**
- **Consult widely on surgical protocols including anaesthesia and analgesia in the study species.**
- **Recognize that wild animals need, and are entitled to benefit from, appropriate prophylactic pain relief and antibiotics.**
- **Monitor post-release morbidity and mortality, especially with respect to surgery and perioperative care; use the results to refine protocols and communicate your findings.**

11.2 External attachment in the field

Every care must be taken to ensure as far as possible that the chosen method of attachment will not abrade skin, scales, fur or feathers (Gedir 2001). Commonly used techniques include collars, pendants or necklaces (e.g. gallinaceous birds, squirrels, otters), neck bands (e.g. geese and swans), backpacks (seals) and harnesses (turtles), leg bands (birds), tail or patagial mounts (birds) (Anderka & Angehrn 1992, Gaunt & Oring 1999, Kenward 2001, Redfern & Clark 2001). Glue, tape such as Tesa™ tape[6] (Beiersdorf WG; Wilson & Wilson 1989) sutures and bolts (for carapaces) are also used to attach devices. Glue is suitable for short-term projects (e.g. between moulting periods) whereas sutures are generally used for studies on rapidly growing juvenile birds where the use of glue is not possible. The sutures gradually pull through the skin as the bird grows, but this method is not to be recommended unless there are no other attachment techniques and there is strong scientific justification for the

[6] For example, see http://www.penguins.org.au/04/andre/content.asp?page=9

study. Sutures should never be used to attach devices to mammals. Harpoons are used to fix devices to the fins or blubber of cetaceans or the muscle of large fish. External attachment techniques for fish frequently involve suturing through skin and muscle and analgesia for fish is poorly understood, which is a cause for concern (see the recent work of Sneddon *et al*. 2003). It is essential to consult organizations such as Concerted Action for Tagging of Fishes (http://www.hafro.is/catag/) for information on current refinements in field fish telemetry and tagging.

Judgement as to the most appropriate attachment method that will cause least discomfort or distress should be made on a case-by-case basis; this will necessitate a comprehensive literature search (see Kenward 2001) and consultation with experts in the field (e.g. Culik & Wilson 1991, Bannasch *et al*. 1994). Research will also be necessary to find out whether external devices are unsuitable for some species and/or behaviours (e.g. small diving birds).

The colour of external components including harnesses, devices and markers should be considered very carefully for studies involving wild animals, in case they affect social status or attract the attention of predators or prey (Keinath & Musick 1993, Cuthill *et al*. 1997, Gaunt & Oring 1999, Redfern & Clark 2001). Red components or identification tags should not generally be used, as they may be mistaken for blood by conspecifics or predators. The likely impact of different colours should be researched for each species.

It is essential that harnesses will eventually become detached from wild animals. Even where data-logging devices need to be retrieved so that data can be obtained, there will need to be a failsafe in place so that the harness will eventually become detached if the animal is not recaptured after a predetermined length of time. One way to achieve this is to use harnesses made from biodegradable materials so that the harness falls off after an appropriate length of time. This is perhaps easiest to achieve in a marine environment, e.g. by using magnesium components or adjacent links of aluminium and stainless steel (Kenward 2001). Another safety option is a 'one break–all release' mechanism so that harnesses are not left hanging from the animal. The most desirable system would be a time-release mechanism (Kenward 2001) and the availability of such equipment should be researched when designing harnesses.

Recommendations:

- **Remember that external attachment methods and markers can seriously impact on behaviour and welfare; research, choose and fit them with care.**
- **Ensure that harnesses will come off at a suitable time following data collection.**
- **Use attachment methods that will not endanger the animal if they break or that have a release mechanism.**

11.3 Releasing instrumented animals to the wild

Subjecting wild animals to procedures and then releasing them into an exacting environment risks both their lives and their wellbeing. It is essential that an expert is present in the field who can make a judgement on the health, welfare and suitability for release of each individual (in some circumstances, this may be the researcher her/himself). Every effort must be made to minimize any risks to animals. **If there is any doubt as to an animal's fitness, s/he should not be released**.

This means that a contingency plan should be in place so that a rapid decision can be made on whether it would be in an unfit animal's best interests to receive veterinary treatment and then be rehabilitated and released at a later date, rehomed to a collection, or killed. It will therefore also be necessary to have the means and expertise to kill animals humanely and containers and transport suitable for moving the species in question to a suitable centre for treatment. For information on the capture and release of wild birds, including those fitted with external devices, see Redfern & Clark (2001).

Release following implantation surgery

The health of wild animals can deteriorate very rapidly in captivity and there is a balance between releasing animals before they have lost condition and holding them for long enough to ensure that they have fully recovered from implantation. If animals are likely to lose condition quickly (e.g. seabirds' feathers can become dirty and abraded on any kind of flooring), it may be necessary to release them relatively soon. This should be of concern and such projects should not be carried out without compelling scientific justification. In these cases, animals should be released at the point of capture in favourable environmental conditions after very carefully checking that:

(i) a full recovery has been made from anaesthesia;
(ii) there are no signs of bleeding, haemorrhage or haematoma;
(iii) no injuries were caused during capture or handling, e.g. broken limbs in small birds;
(iv) analgesics and antibiotics have been administered as appropriate; and
(v) the animal is not in shock or pain. Behavioural and physiological indicators of shock and pain in the species should be thoroughly researched and a checklist should be prepared for field use. If necessary, an experienced veterinarian or other relevant expert should accompany the investigator to assist with assessing animals.

There are, however, other conditions that will affect the balance relating to when an animal should be released. For example, an incubating bird may be released onto her nest while still under the influence of the anaesthesia. She can then recover in familiar surroundings and is less likely to desert the nest. The welfare of any dependent young animals should also be taken into account. If trapping and instrumenting lactating females, care should be taken that each female returns to her young within an appropriate time. This may mean increasing trap surveys and reducing the period of time that animals are held for when their offspring are very young.

If animals can be held for longer periods (e.g. days), clinical signs that should be monitored before release include signs of infection (e.g. raised temperature), haematological changes, superficial or other injuries, appetite, eliminatory behaviour, and any other possible interferences with normal body function as described elsewhere. In general, normal circadian rhythms should have been re-established and animals prepared to feed in captive conditions should be taking appropriate amounts of food and water.

Release following external device attachment

Animals are usually released immediately after devices have been attached to them. Points (iii) and (v) above also apply in such cases; so does point (i) if it has been necessary to anaesthetize or sedate the animal to fit the device. Also note that immobilizing drugs will inevitably have side-effects that may not always be predictable in wild animals; for example, repeated immobilization has been found to have a negative impact on fertility in the black rhino *Diceros bicornis* (Alibhai *et al*. 2001).

Recapture

It will often be necessary to recapture animals, for reasons of science and/or animal welfare. Thorough consideration must be given at the project planning stage to the methods used to recapture animals, the likelihood that they will succeed and the consequences for both animal welfare and the science if individuals are not caught again. All of this should form part of the harm–benefit assessment and a pilot study may be necessary if there is any doubt as to the potential to recapture animals.

Recommendations:

- **Never release an animal if you suspect that her or his fitness has been significantly compromised.**
- **Have a contingency plan in place for animals needing veterinary treatment or euthanasia.**
- **Carefully consider the duration of post-surgery captivity; plan pain management and set out health checklists accordingly.**
- **Consider and address the welfare of juvenile, dependent animals when deciding when to release parent animals.**

- **Give serious thought to recapture methods and their probability of success, carrying out a pilot study if necessary.**

12 Writing up projects involving telemetry

It is essential that good practice with respect to surgical protocols, especially pain management, is disseminated by every means possible. The Working Group believes that refinements in both procedures and husbandry should be included in the materials and methods sections of scientific papers and should not be marginalized or segregated—see www.lal.org.uk/telemetry/ for a worked example. Method sections of scientific papers, posters and talks should include details of at least the following:

- Age, mass and sex of animals
- Husbandry and care, including environmental stimulation
- Selection of animals and training if appropriate
- Duration of preoperative monitoring and variables used; preparation for surgery
- Anaesthesia
- Pain management: pre-emptive analgesia; postoperative analgesia; doses and duration; how duration was decided
- How pain and distress were recognized; clinical signs denoting specific actions; frequency of monitoring
- Prophylactic antibiotics
- Device mass, dimensions and shape
- Surgical techniques; device location
- Success rate
- Assessment of the impact of the device on the animal, especially for wild animals[7]
- Any technical problems and how they were solved

It is commonly believed that such detail is inappropriate and that journal editors would refuse to include more information on refinement due to lack of space or because it is not the convention. The Working Group believes, however, that it is the responsibility of those using animals to make a case for including more detail, on ethical, scientific and welfare grounds. Information on husbandry and care can also often be summarized so that length is not an issue (GV-SOLAS 1985, Morton 1992, Smith *et al*. 1997). Details of refinements should be included in paper titles and abstracts wherever possible, and attention should be drawn to this by using relevant keywords such as refinement, reduction, analgesia or enrichment. This will encourage database compilers to use keywords indicating that the paper includes information that will enable others to refine procedures and/or husbandry.

Recommendations:

- **Include comprehensive information on how suffering was reduced and welfare improved when writing up studies involving surgery or when presenting posters or talks.**
- **Always include full details of anaesthesia and analgesia.**
- **Give a list of clinical signs that were key to decision making with respect to humane endpoints, continued provision of analgesia etc.**
- **Challenge any requests to remove such information.**
- **Try to mention refinement and reduction in titles and abstracts; reflect this in your choice of keywords.**

13 Keeping up with new developments

New developments in telemetry could lead to refinements in procedures or reductions in animal numbers, so it is essential to ensure that progress is monitored and techniques and equipment updated as appropriate. There are a number of means to achieve this, including user groups (for both literature and user meetings), the International Society for Biotelemetry (http://baby.indstate.edu/isb/frames/), manufacturers' newsletters, and the World Wide Web. The IMPI report (2002) is also a useful starting point (http://www.impi.org.uk/i3r_v2_jul2002.pdf). It is, however, important to use information from the web or user groups very critically, as it may not be

[7]Only 10% of marked-animal studies published in major journals in 1995 included evidence that tag impact had been considered (Murray & Fuller 2000).

properly refereed or refereed at all. Uncritical use could lead to welfare problems or undermine scientific validity. Examples of keywords recommended for searching the literature on refinement include ANIMAL HUSBANDRY, ANIMAL CARE, ENVIRONMENTAL ENRICHMENT, ANIMAL WELFARE, ANIMAL WELLBEING, STRESS, DISTRESS, PAIN, PAIN MEASUREMENT and PAIN REDUCTION (IMPI 2002).

Recommendation:

- **Ensure that you are doing all you can to monitor developments in telemetry, for example by joining and participating in appropriate user groups and regularly checking the literature and the web for potential refinements.**

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Appendix 1 Selected useful information

Recommended reading

General

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Training aids

Bell Isolation Systems Ltd
Units 12 & 13, 32 Sycamore Road, Dalkeith, EH22 5TA, Scotland, UK
Tel +44 (0) 131 654 5725, Fax +44 (0) 131 654 5726
info@bell-isolation-systems.com
www.bell-isolation-systems.com/simulators.htm

Braintree Scientific, Inc.
PO Box 850929, Braintree, MA 02185-0929, USA
Tel (1-781) 843 2202, Fax (1-781) 843 7932
Info@braintreesci.com
http://www.braintreesci.com/

Appendix 2 Score sheet for postoperative monitoring of rats following laparotomy and telemeter placement

RAT NO:		**ISSUE No:**					
MICROCHIP NO:							
DATE OF SURGERY:		**PRE-SURGERY WEIGHT:**					
DATE							
DAY							
TIME							
FROM A DISTANCE							
Twitch**							
Stagger/fall (any loss of balance)**							
Full/partial back arch**							
Writhe**							
Inactive							
Not inquisitive or alert							
Isolated							
Starey coat							
ON HANDLING							
Not eating							
Not drinking							
Bodyweight (g)							
% change from start							
Body temperature (°C)							
Discharge eyes/nose							
Coat wet/soiled							
Diarrhoea/faecal pellets* +/-							
Wound OK? Open/infected							
Number of sutures/stapels							
Dehydration: skin pinch							
Audible vocalisation							
Other signs noted							
SIGNATURE:							

Special husbandry requirements:
Monitor animal twice daily for 1st week until wound healed
Offer soaked pellets and unsoaked, appetising food e.g. grapes, Cocopops^{TM} (Kelloggs) on the floor
Scoring details to be ascertained
*D for diarrhoea, P for faecal pellets, the number may also be noted
Humane endpoints and actions
**Additional analgesia is required if the combined frequency of 'twitch', 'stagger/fall', 'back arch' and 'writhe' exceeds 10 occurrences in a 10 min observation period (see Roughan & Flecknell 2001). In this event, contact the veterinarian.