

Animal experimentation in Malta: regulatory processes and future perspectives

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Abstract

Prior to Malta's accession to the European Union (EU) in May 2004, new legislative processes regulating the use of animals for scientific research purposes were adopted in line with the provisions found under the European Union Council Directive 86/609/EEC. The scope of these regulations is to protect animals used or intended to be used in scientific experimental procedures which may cause pain, suffering, distress or lasting harm, using evaluation procedures that promote refinement, reduction and replacement techniques.

Introduction

Animal experimentation has played a fundamental role in developing methods of prevention, diagnosis and treatment of various human and animal diseases. Additionally, the use of animals has been indispensable for testing the mode of action, potency and safety of drugs and medical equipment, production of life-saving vaccines, assessment of hazardous chemicals, and for education and training in healthcare technologies. Indeed, current justification for animal experimentation rests partly on numerous examples of its contribution to medical progress.

Keywords

Animal experimentation, laboratory animal legislation, animal welfare and ethics

The use of research animals for experimental purposes has also been a major ethical issue in the medical and scientific community especially in these last decades following the increase in international public concerns about the welfare of animals. As a result, the use of laboratory animals for experimental purposes is extensively regulated at European, pan-European and national levels. This ensures that scientific research using animals has realistic and achievable aims of increasing scientific understanding, either for the benefit of humans, or of animals, or both. Such regulatory processes are also necessary so that experimental protocols are properly evaluated and justified.

Regulatory processes

In Europe, especially among EU member states, the need to regulate animal procedures led to the implementation of legislative processes aimed at encouraging and supporting the development, validation and acceptance of methods needed to reduce, refine or replace (3Rs) the use of laboratory animals.¹ The most important of these is EU Council Directive 86/609/EEC, covering various issues related to animal welfare such as handling, housing conditions and transport.² This Directive is binding to all member states and thus it had to be included in the national legislation. This Directive is currently under review by the EU Council due to its limitations in addressing techniques that are now available to the scientific research community such as the use of transgenic animals, cloning and xenotransplantation. Animals killed for their tissues and organs, including those used for the development of *in vitro* methods, are equally excluded. Furthermore, Directive 86/609/EEC does not mention the need of having ethical evaluation procedures prior to authorisation of animal experiments or the explicit use of the 3Rs. Following a European-wide campaign, EU-member states agreed in 1997 to include a protocol on the protection and welfare of animals (Amsterdam Treaty) formally recognising animals as sentient beings.³ This protocol was an important step in imposing an obligation on EU-member states to take account of animal welfare considerations when formulating and implementing the Community's agricultural, transport, internal market and research policies.

Compared to other countries, the use of animals for scientific research purposes in Malta has a relatively short history. In 1993, a group of researchers coming from different medicine-orientated fields working within the Faculty of Medicine and Surgery at the University of Malta drafted a document proposing

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the establishment of a small-animal housing facility on campus including research facilities that cater for both *in vivo* and *in vitro* research work.⁴ Since the authors were trained in higher institutions in the United Kingdom (UK), and no local legislation was in force at the time, it was agreed that all experimental procedures using laboratory animals should conform to the UK Animals (Scientific Procedures) Act of 1986.⁵

Prior to the formal acceptance of Malta as a European Union member state, new legislation was implemented in the form of the Malta Animal Welfare Act (Act No XXV, 2001) followed by Legal Notice 263 (Animal Experimental Regulations, 2003).^{6,7} The Malta Animal Welfare Act was mostly intended to establish and consolidate the protection of animals kept for work, sport, companionship and food. However, it also includes a number of articles that specifically address areas involved in biotechnological research and animal experimentation. It specifically calls for the establishment of an Animal Welfare Council composed of individuals directly appointed by the minister for Rural Affairs and Environment upon recommendation of associations or groups which, in the opinion of the minister, are representatives of the relevant associations or groups (Table 1). This council may also appoint subcommittees that discuss and decide on specific matters such as farm animal housing systems, biotechnology and animal experiments. In the section dealing with animal experimentation, the Malta Animal Welfare Act stipulates that the minister for Rural Affairs and Environment may issue other regulations for procedures to be followed in the case of experiments involving animals (Article 36, Sub-article 1). Indeed, the Malta Animal Welfare Act was later supplemented with Legal Notice 263 of 2003 which specifically laid down legal regulations that need to be followed to conduct animal experiments in Malta. The scope of this legal notice was also to fully implement the provisions found under the European Union Council Directive 86/609/EEC. For the first time in Malta, individuals making use of research animals for scientific purposes had to seek authorisation by completing an application form for review and acceptance by the Animal Welfare Council. Most importantly, these regulations state that:

- (i) experimental procedures using animals can only be carried out by authorised individuals, or under direct responsibility of an authorised person and such authorisation will only be granted to individuals deemed to be competent by the relevant authorities (mainly the Veterinary Services within the Ministry for Rural Affairs and Environment),
- (ii) Breeding and supplying establishments have to be registered with the Veterinary Services and that such establishments should also specify the person in charge of the establishment who shall be competent to administer or arrange for suitable care for animals of the species bred or kept in the establishment. Records of the number and strain of animals kept and/or supplied should be kept together with details of the recipient,

- (iii) Establishments in which research animals are used for experimental purposes (user establishments) should be registered with the Veterinary Services, have a person responsible for the care of the animals, have adequately trained staff, have arrangements for provision of veterinary advice and keep records on the number of animals used and procedures conducted,
- (iv) Persons who carry out the experimental procedures, or take part in them, or take care of animals used in procedures shall have had appropriate education and training.

In order to avoid unnecessary repetition of experimental procedures required by law on health and safety, Legal Notice 263 stipulates that where practicable, results of procedures carried out in the territory of another party would be recognised. Procedures carried out for the purpose of education, training or further training of professions or other occupations, including the care of animals being used or intended for use in experimental procedures are restricted to only those absolutely necessary and only if the objective cannot be achieved using non-animal methods. The competent government authorities should also be notified and on authorisation, the procedures must be carried out by an authorised person who will be responsible for ensuring that the experimental procedures comply with the legal requirements. These regulations are in line with the concept of the 3Rs in trying to reduce the number of animals used for scientific experimentation.

Laboratory animal research at the University of Malta

Experiments using laboratory animals have always formed an essential part of scientific research at the University of Malta, both at undergraduate and postgraduate level. With the introduction of modern research techniques using *in vivo* and *in vitro* models there was an increasing need to set up a proper animal housing facility on campus in conformity with internationally-accepted standards together with the adoption of internal regulations for proper conduct of animal experimentation. Prior to the issuing of the Malta Animal Welfare Act, various research projects making use of small laboratory animals (mainly mice and rats) were completed by staff trained in animal care and welfare during their postgraduate education at foreign academic bodies. However, with the introduction of the much needed legislation, animal experiments have to be approved and authorised by the Malta Animal Welfare Council acting in accordance with the Malta Animal Welfare Act and Legal Notice 263. One of the requirements is the need for the University of Malta to be registered / licensed as a user and breeding (in the case of in-house breeding) establishment.

Future perspectives and recommendations

There are various aspects that should be considered in developing a strategy aimed at conducting ethically sustainable and scientifically valid use of animal research in Malta.

Table 1: Composition of the Malta Animal Welfare Council (AWC) according to the Malta Animal Welfare Act (Act Number XXV of 2001). At present the AWC does not require representation from the scientific, ethical and legal backgrounds in areas relevant to the use of animals for experimental research purposes.

The Council consists of:

- (a) The Director for Veterinary Services, who shall be the chairman
- (b) A representative from the Ministry responsible for Veterinary Services
- (c) One veterinary surgeon, employed in the public service, with experience in animal health medicine
- (d) One veterinary surgeon, employed in the public service, with experience in farm animals' matters
- (e) Two persons to represent the interest of animal welfare groups
- (f) Two persons to represent the interests of breeders and animal sports groups.

The Animal Welfare Council

It is within the scope of any user establishment in Malta to have a local Animal Welfare Council functioning efficiently as stipulated in the Malta Animal Welfare Act. It is only through the vetting and approval of this Council, following the advice of its nominated subcommittees, that animal experimentation can be conducted in Malta. This Council also acts as an advisor to the relevant governmental authorities on several issues concerning care and welfare of animals. The members composing the subcommittee entrusted to evaluate research projects making use of laboratory animals should also be selected on grounds of expertise and technical knowledge. This should help to eliminate misunderstandings that may arise between the scientific community and the animal rights' group representatives that currently make up a good proportion of the subcommittee. Ideally, the scientific community should be equally represented in order to insure that all use of laboratory animals is scientifically justified. Owing to the various ethical issues involved in the use of animals for research purposes, ethical and legal representation should also be considered as part of the evaluation process.

Improving the University of Malta animal research infrastructure

Being a key player in developing a strategy towards responsible use of animals for scientific research, the University of Malta should seek ways of improving the infrastructural resources which currently are very limited and fall short of fulfilling the technical and legal requirements that are necessary to conduct animal research in accordance with Schedule A of Legal Notice 263. It would be advisable that animal housing and research facilities involving the use of laboratory animals

be centralised in a building designated for such use. This building should include holding rooms, surgery rooms, and laboratories intended for both *in vivo* and *in vitro* research work conducted by the various interested University departments. Such a building should be designed using European-accepted guidelines and accredited by international bodies such as The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC Intl.). Since the financial costs involved in the set-up of such facilities would be significant, it would be appropriate to identify an already existent site at the University grounds and convert it in a manner that fulfils the research needs of the local scientific community according to international standards and legislation. In this respect, European funding should also be sought as a means of tapping financial resources in this sector. This, together with the technical expertise already available, would facilitate the participation of the Maltese scientific community in EU-related collaborative projects involving the use of animal models.

Education

Research involving the use of animals plays an important role in scientific and medical advancement and every present day protocol for the prevention, treatment, cure and control of disease is based on knowledge obtained through animal research. The essential need for animal research is also recognised and supported by medical societies and health agencies worldwide.

Currently, the various issues involved in animal research including the different models used to study disease do not form an essential and integral part of the curriculum of medically or scientifically-orientated undergraduate or postgraduate training programmes. This may be considered as a disadvantage to those students who will eventually pursue their careers in the field of medical research. Furthermore, pharmaceutical companies world-wide invest considerable amounts of their financial resources in research and development of new pharmacotherapeutic agents which at some stage involve responsible use of research animals. Undergraduate courses that may benefit include those in health and life sciences. Training at postgraduate level in specific areas within the various departments of the Faculty of Medicine and Surgery, Faculty of Science as well as the Institutes of Health Care and Agriculture should also be of benefit.

Professional training

The Malta Animal Welfare Act together with Legal Notice 263 stipulate that individuals making use of research animals for experimental purposes should be adequately trained in the various aspects of animal care and welfare in order to be granted the necessary authorisation. Unfortunately, there is no mention of the type and level of training required. It is expected that such training would include legal and ethical aspects, husbandry, animal handling techniques, disease-control, euthanasia, experimental methodologies and surgical skills.

The University of Malta can play an important role in offering the proper education needed in this area. This can be done by offering training courses, initially validated and assessed by international bodies, leading towards proper accreditation and recognition by the local authorities. These training courses may also be organised on a part-time basis and to external parties such as the pharmaceutical industry or members of the general public who wish to increase their knowledge of laboratory animal technology.

Ethical issues

Although the EU Council Directive 86/609/EEC contains no specific requirement for prior ethical review of proposed animal studies, it is now widely accepted that, if the content of animal experimentation raises ethical concerns, an ethical review process should be involved. As a result, most European countries have effective and mandatory national structures that address the various ethical issues that arise in animal research. Although the University of Malta has set up a Research Ethics Committee whose guidelines became effective in October 2004, these guidelines only regulate research involving human subjects and only apply to university staff and students.⁸ Therefore, the University of Malta lacks the necessary structure to review and decide on ethical considerations arising from experiments in which research animals are used and thus, such decisions fall within the purview of the Animal Welfare Council or one of its subcommittees. It is therefore advisable for the University of Malta to either appoint a committee evaluating ethical issues involved in animal research prior to submission for research authorisation to the relevant government authorities or appoint an individual with scientific and ethical expertise in this area on the University of Malta Research Ethics Committee. All ethical review processes should not only consider the legal aspects and the implementation of the 3Rs during the project evaluation phase prior to submission but also ensure that the law is adhered to throughout the whole course of the research programme.

The application process

In order to conduct animal experimentation procedures in Malta, interested parties need to apply to the Animal Welfare Council by filling an application form which will then be discussed by the Council or one of its subcommittees before authorisation is granted. Details to be included in the application form include:

- (i) Applicant's information including qualifications, the period for which the licence is required, the address of the user establishment and the details of the person who has responsibility for animal care within the user establishment,
- (ii) Details of the experimental activity involved including the objective (research and/or teaching) and type of procedure (pharmacokinetic, surgical, forensic etc), whether alternative techniques are available and the principal technique to be utilised,

- (iii) General description of the research study including its significance, scientific questions addressed, general goals and endpoints,
- (iv) Types and total number of animals to be used including source of animals and projected total number per annum and for the overall duration of the project,
- (v) Use of anaesthesia together with the overall category of pain expected,
- (vi) Details on post-operative care, techniques used to minimise pain and likely adverse effects,
- (vii) Research experience and competencies of the applicant,
- (viii) Details on the animals to be used and the supplier.

Although the application form addresses most of the details required to conduct animal experimentation according to the local legislation, it does not contain any ethical evaluation process or a requirement for detailed breakdown of the different procedures involved at particular stages of the project together with the corresponding animal numbers and pain severity limits. Furthermore, there is no direct mention of whether the research work would involve the use or production of transgenic animals. This is particularly important since the Malta Animal Welfare Act specifically prohibits the use or production of genetically modified experimental animals without prior and direct authorisation from the minister for Rural Affairs and Environment. Also, the application form does not require information regarding animal housing and welfare conditions or whether the animals will be deprived of food and water as part of the experimental protocols. Although local legislation requires that both the user and breeding establishment should be authorised, there is no mention of any certification number. Interestingly, although the application form is directed in getting details regarding the research project, it is referred to as 'Application form for user establishment licence' rather than 'Application form for project licence.' Indeed, no application forms specifically designed for user and breeding establishment are available from the authorities and the procedure by which these licences are granted is not specified in the law. It is therefore advisable that separate application forms, depending on the type of licence requested (user/breeding/project), should be available.

Strengthening collaborations with EU partners

Although the use of animals for research purposes is a fundamental tool in scientific advancement and understanding, it is not without controversy. Even though most people may see the benefits of such use, the question of how to protect animals from being used in unnecessary experiments remains a valid and sensitive issue in science, politics and society in general. The main goal of any legislative process, especially in EU member states, is to establish a uniformly high standard for the use of experimental animals using the 3Rs concept. Various approaches are used to achieve this goal. Apart from the legislative process, the EU also encourages collaboration

between member states in order to increase the knowledge for both ethically sustainable and valid use of laboratory animals in research. One such instrument is the European Cooperation in the field of Scientific and Technical research (COST) Action B24 – Laboratory Animal Science and Welfare, of which Malta is one of the signatories and member of the Management Committee.⁹ Representatives from various EU-member states meet regularly to discuss and advice on regulatory guidelines and recommendations involving the use of laboratory research animals which go beyond the minimum required standards. These types of actions also fund researchers from different countries to participate in exchange programmes aimed at strengthening collaboration between participating countries. The aim of the Short-Term Scientific Missions (STSM) is to contribute towards the scientific objectives of the COST Action. Through collaboration with its European partners, Malta does not only ensure an effective mechanism of dialogue between the different stake holders but also identifies opportunities for progress in areas in need of development.

Conclusion

Although the use of laboratory animals for research purposes in Malta is limited in size compared to other European countries, every effort should be made in encouraging this scientific discipline especially in research-based institutions such as the University of Malta. This can only be achieved through collaborations between the major stake-holders, particularly the local government authorities and the scientific community. The authorities should also ensure that the Animal Welfare Council functions effectively allowing research institutions such as the University of Malta to conduct responsible research with animals in full compliance with the Malta Animal Welfare Act (2001) and Legal Notice 263 (2003).

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