

Quality management for the international transport of laboratory animals

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Summary

Increased collaboration between investigators at different institutions has increased the number of laboratory animals being transported. The current system of laws and regulations governing animal shipments is inconsistent and government agencies often have areas of overlapping regulatory management. Furthermore, the lack of industry-wide shipping standards and good practices contributes to confusion among those responsible for shipment. One answer to these quality control issues would be the establishment of independent, industry-regulated 'good practices' for animal transport, similar to those used in laboratories for experimental design. These good practices could be based on the existing International Air Transport Association Live Animals Regulations, with contributions from representatives of the specialties involved. Additionally, quality control under the current system of patchwork regulations could be improved if each institution, both academic and commercial, would designate a single point of contact to follow each shipment from start to finish.

Keywords

Air transportation, Animal, Animal welfare, Humane transport, Laboratory, Transportation, Regulation, Shipment, Welfare.

Gestione della qualità nel trasporto internazionale degli animali da laboratorio

Riassunto

La crescente collaborazione tra i ricercatori e le diverse istituzioni ha incrementato il numero di animali da laboratorio trasportati. L'attuale sistema legislativo e le norme che regolano le spedizioni di animali sono contraddittorie e spesso le agenzie governative si trovano di fronte a norme che si sovrappongono. Inoltre, la mancanza di standard generali nell'industria delle spedizioni e di buone pratiche contribuisce alla confusione sulle responsabilità nell'ambito delle spedizioni. Una risposta alle tematiche del controllo di qualità potrebbe essere l'istituzione di "buone pratiche" per il trasporto animale indipendenti, industry-regulated, simili a quelle utilizzate nei laboratori di sperimentazione. Queste buone pratiche potrebbero basarsi sulla legislazione per il trasporto di animali vivi dell'International Air Transport Association Live animals Regulations, con il contributo dei rappresentanti dei settori di competenza. Inoltre il controllo di qualità nell'attuale confuso sistema di norme potrebbe essere migliorato se ogni istituzione, sia accademica che commerciale, indicasse un singolo punto di contatto che seguisse ogni spedizione dall'inizio alla fine.

Parole chiave

Animali da laboratorio, Benessere, Benessere animale, Regolamenti, Spedizione, Trasporto Trasporto aereo, Trasporto umano.

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Introduction

Due in part to genome projects and transgenic technology, animal-based research programmes have experienced exponential growth in recent years. As investigators collaborate, the numbers of animals transported between institutions has increased. At the same time, the number of carriers (particularly air carriers) that allow animal transport is mostly static. The situation for non-human primates is even more critical, as few carriers will transport non-human primates destined for research. This creates a particular hardship for researchers who utilise non-human primates. Although the humane transport of laboratory animals has always been of concern, these factors make the case for standardised shipping guidelines and uniform training and good practices even more important.

The United States National Center for Infectious Diseases of the Centers for Disease Control and Prevention and the National Institutes of Health asked the Institute for Laboratory Animal Research (ILAR) of the National Research Council to convene a committee to address problems associated with the transportation of research animals. The report of this committee, *Guidelines for the Humane Transportation of Research Animals* (6) covers all of the aspects of animal transportation in great detail and provides recommendations for improvements to the system. Much of the information in this section is taken from this ILAR report.

Issues

Regulations

European Union

Transportation of research animals in the European Union is governed by three related policy areas, namely:

- Consumer Policy Treaty Articles 95 and 153
- Public health Treaty Articles 95, 152 and 300
- Food Safety, Animal Health, Animal Welfare, and Plant Health Treaty Articles 37, 95, and 152.

These regulations are enforced by the Health and Consumer Protection Directorate General.

United States

In the United States, five agencies have overlapping responsibility for nine federal laws governing the transport of animals and animal tissues, namely:

- Animal Welfare Act (PL 94-279)
- Lacey Act
- Endangered Species Act
- Division on Global Migration and Quarantine
- Etiologic Agent Import Permit Program
- Infectious Substances Program
- Radioactive/Poisonous Materials Program
- 42 CFR 70.2
- 21 CFR 1240.30.

In addition, individual carriers may enforce their own guidelines based on these laws and statutes.

International

Regulations for the international transportation of laboratory animals are in part governed by various treaties and agreements. However, each country may also have its own laws and guidance. The International Air Transport Association (IATA) *Air Cargo Tariff Book* (23) provides information regarding international documentation and import requirements, but the shipper is well-advised to check each individual country's website or consulate as well.

The Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), also known as the 'Washington Convention', established a permit system for regulating endangered plants and animals which is enforced in 169 countries. Non-human primates are a species commonly used in research that are covered by CITES.

Good practices

Good practices in laboratory animal transportation, such as good laboratory practices (GLPs), are detailed and standardised guidelines that are to be followed precisely by all parties involved in the animal shipment process to ensure maximum animal safety and comfort during transport. Science-based good practices in animal handling and transport are

discussed in a number of publications, including the Animal Transportation Association (AATA) *Manual for the Transportation of Live Animals* (2), IATA *Live animals regulations* (LAR) (22) and the Report of the Transport Working Group Established by the Laboratory Animal Science Association (31). Good practices may include guidelines as described below.

Stress

The uniform, familiar environment the animal normally inhabits is changed almost entirely during shipment. This makes transportation, even though it lasts at most a few days, an acutely stressful event for the animal being transported. Less information is available regarding the physiologic effects of transport on common research animals than for agricultural animals, but a corollary can be drawn between the two. During shipment, all animals exhibit some behavioural change, neuro-endocrine and peripheral endocrine responses, and activation of homeostatic mechanisms, but the extent of these responses vary significantly according to age, species and strain.

Stress may be minimised by limiting the amount of time that animals are removed from their normal environment and providing some aspect of the home environment if possible, e.g. providing familiar bedding. In addition, prior to transportation, it may be beneficial to expose the animal to certain conditions it may encounter during transport, such as unusual sources of food and water (e.g. gel packs) or the primary enclosure.

Thermal regulation

Maintaining a temperature range appropriate for the species in question is as important during transportation as it is in the normal housing environment. Thermal stress is the major factor in animal mortality during transit and the single most important risk factor for the safe and humane transportation of animals. Caging type, the amount of space allocated within the cage and how the shipping containers are stacked within the cargo hold, all contribute to temperature equilibrium.

A number of sources, including the United States Animal Welfare Act and IATA's LAR, provide information about temperature ranges for individual species. Table I, excerpted from *Guidelines for the humane transportation of research animals* (6), is an excellent compilation of thermoregulation data for the animal species commonly used in scientific research.

Food and water

Many animals refuse food and water during transport, which contributes to the typical stress response of weight loss. Additionally, provision of food and water can be difficult and may actually undermine attempts at thermal regulation if the water spills and the animal becomes wet and chilled. Therefore, food and water may not be of any benefit and may actually be detrimental, during short trips.

During periods of longer transport, regulations often require that food and water be provided. For example, the United States Animal Welfare Act details feeding requirements by species and age: dogs and cats over 16 weeks of age and non-human primates over one year of age must be offered food once every 24 h and water once every 12 h.

Small and young animals lose more heat, require more calories per unit of body mass and become dehydrated more rapidly than larger animals. Therefore, food and water must be available to small and young when transportation lasts more than a few hours. Gel moisture sources can provide hydration and prevent water spills. However, an additional food source may be necessary as these are not nutritionally complete.

Social interaction

As most trips are of short duration, it is less important to provide social housing than it is to ensure that the animals being shipped are not within sight of prey or predator animals; e.g. sheep transported with dogs when the animals can see each other.

Handling

Socialisation of animals prior to shipment will help minimise their stress during transport.

Table I Thermoregulation data on common research animal species

Species	Average rectal or intraperitoneal temperature (°C)	Ref.	Thermo-neutral zone (°C) ^(a)	Ref.	Lowest tolerated ambient temperature ^(b) (°C)	Ref.	Highest tolerated ambient temperature (°C)	Ref.
Mouse	36.5 ± 1.3	18	26 to 34	11, 19, 27	-5 (3 h)	27	34 (2 to 3 h)	27
Rat	36.7 ± 0.9	19	26 to 33	13, 14, 32, 33	-15 (3 h)	7	34 (100 min)	12
Guinea-pig	39.2 ± 0.7	19	28 to 30	9	-20(1.5 h)	20	36 (30 min)	9
Rabbit	39.5 (38.6 to 40.1)	29	15 to 20	5	-10 (2 h)	16	32.2 (2 h)	4
Hamster	36.8± 0.2	25	25	25	-30 (1h)	28	32 (60 to 80 min)	25
Rhesus macaque	39.1 (37.9 to 40.0)	24	24.7 to 30.6	24	15 (1 h)	24	40.0 (1 h)	24
Dog	38.9 (37.9 to 39.9)	29	20 to 26	5	-35 (30 min)	10	35.0 (2 h)	3
Pig	39.2 (38.7 to 39.8)	29	16 to 23	21	-20 (indefinitely)	8	35 (indefinitely)	8
Cat	38.6 (38.1 to 39.2)	29	35 to 38	1	-5 (1.5 h)	17	35 (1.5 h)	1
Sheep	39.1 (38.3 to 39.9)	29	21 to 25	5	-	-	-	-
Beef cow	38.3 (36.7 to 39.1)	29	-18 to 23	15	-	-	-	-
Dairy cow	38.6 (38.0 to 39.3)	29	-15 to 26	15	-	-	-	-
Stallion	37.6 (37.2 to 38.1)	29	5 to 25	26	-	-	-	-
Mare	37.8 (37.3 to 38.2)	29	5 to 25	26	-	-	-	-
Goat	39.1 (38.5 to 39.7)	29	13 to 21	5	-13 (indefinitely)	30	-	-

(a) Thermo-neutral zones can vary by strain, age and reproductive or health status

The measurement of an animal's thermo-neutral zone may also be influenced by the room temperature and caging condition of the animal's regular housing

(b) That results in no substantial change in core temperature over the time period indicated in parentheses

In some cases, lowest and highest tolerated ambient temperatures were determined in acclimated animals

Source: *Guidelines for the humane transportation of research animals* (6)

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Additionally, carrier personnel should exercise care when moving, loading, or unloading animal shipments. The Animal Welfare Act states that handlers 'must avoid causing physical harm or distress' to the animal and sets forth specific handling requirements for each species.

Emergency procedures

In animal transportation, 'emergency' runs the gamut from an escaped animal to a flight delay. Both the shipper and the carrier should have plans in place to deal with any

emergency that may arise. Shipper and carrier should maintain communication throughout the event. Qualified, trained personnel, preferably a licensed veterinarian, should be available to make and carry out decisions regarding treatments and/or euthanasia. Appendix B, Section II of IATA's LAR details appropriate responses to various emergency situations.

Training

In 2002, a report of the American Veterinary Medical Association-United States Department

of Agriculture animal air transportation study group evaluated the training programmes of several United States air carriers with regard to animal transport. Although most carriers provided good initial training for their employees who may have contact with animals in transit, continuing education was inconsistent.

Whether animals are shipped by regular or specialised carriers, the rules for employees are much more complex than for handling ordinary baggage or cargo. Staff handling animals must be trained in a number of areas, proper loading and unloading, veterinary issues (such as how to recognise distress or illness), when a veterinarian should be notified, animal husbandry and governmental regulations regarding animal observation, food, water and shelter. In addition, the sheer amount of paperwork required can be daunting. All of this requires specialised and continuing training which should be included in the good practices guidelines.

Biosecurity

The increased shipping of valuable transgenic mice, some immunocompromised, and the need to maintain their biological status has resulted in a greater need for proper transportation practices. Barrier containment-level shipping containers, pathogen testing, adequate disinfection procedures, appropriate personnel protective equipment (PPE) and segregation of different animal shipments are critical aspects of good practices. Close contact between humans and animals during transport increases risk of zoonoses. For example, there are reports of rodents and rabbits with tularemia, salmonella and human lymphocytic choriomeningitis virus. Special consideration should be given to non-human primates, as herpes B (*Herpesvirus simiae*), dengue, and Ebola are transmissible to humans through aerosols, animal bites, direct contact or equipment that has come into contact with infected body fluids or tissue. Good practices will minimise the risk of transmission of infectious pathogens to humans and animals.

Conclusion

Primary contact

The ILAR Committee on Guidelines for the Humane Transportation of Laboratory Animals recommends that all research institutions, academic or commercial, designate a single individual to be responsible for ensuring the safe shipment and receipt of research animals. Washington University in St Louis, Missouri, averages 43 animal shipments per month, both national and international. In 1997, we implemented the dedicated shipment coordinator position. Having a single point of contact has centralised and streamlined our animal shipment process, improved communication and freed veterinary time.

Declining availability of air transportation for non-human primates

As most United States domestic airlines have banned the transport of non-human primates destined for research facilities, the ILAR Committee on Guidelines for the Humane Transportation of Laboratory Animals recommends that a working group associated with the United States National Primate Research Centers encourages the development of a reliable ground transportation network. Non-human primate users and veterinarians in the European Union may find it helpful to form a similar working group. Additionally, an international working group might be established to research and recommend alternative forms of transportation (e.g. dedicated shippers, chartered flights) for these animals.

Harmonisation of regulations and good practices

Overlapping regulatory authority and burden would be minimised if a single entity provided animal transportation oversight. Regulations could likewise be improved to avoid inconsistencies and thus be more comprehensible.

If government regulators are unable to collaborate and produce a cohesive set of regulations for animal transport, perhaps a working group of the various experts could

agree on across-the-border standardised regulations and good practices, similar to those established by IATA in the LAR.

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