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The Development of Laboratory
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Legislation and the Consummation

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The Development of Laboratory Animal Science and Animal Care of Legislation and the Consummation

Abstract: Laboratory animal science is the use of non-human animals in experiments to obtain new knowledge and new technologies in biomedical research and testing. In order to develop science and technology, the human carried out a large number of animal experiments, these experiments greatly expanded the vision of related research field, and make a great contribution to human beings. Meanwhile, animal experiments also bring us a certain extent of negative effects. Countries around the world have adopted legislative measures to regulate behavior of animal experiments, but in the process of legislation and enforcement are not wholly satisfactory. On the basis of present situation of laboratory animal science and existing problems, with the comparison of animal welfare act between Europe and China, the author puts forward the ideas of perfecting experimental animals' laws and its enforcement proposals.

Key words: Experimental Animals; Animal Welfare Act; Consummations of Legislation

I. The Development of Animal Experiments and Laboratory Animal Science

Animal experiments refer to the use of non-human animals in experiments to obtain new knowledge and new technologies in biomedical research and testing. Animal experiments have a long history and great quantity in medicine and scientific researches, and in many fields, especially in medicine, animal experiments made great contribution. For instance, with the help of animal experiments, we find the way to cure the infantile paralysis, polio, influenza, and pneumonia; those diseases were brought great pain to human beings. Even the way in which to use mice as specimens to treat leukemia had made great progress. Particularly, this kind of examples can be found in the history of the Nobel Prize winners' list. For example, 1901 Nobel Prize winner Emil Adolf von Behring's guinea pig experiments discovered an antitoxic serum for diphtheritis. In 1923, John James Richard Macleod who developed yellow fever vaccine with an experiment by dogs, rabbits, and fish, etc.

Now, we are facing a new technology revolution age. Biological engineering, microelectronics technology, new materials, and new energy are booming. These are all indicating that we are heading to the era of life science. We need laboratory animal to explore the original of life, to reveal the secret of genetic, to conquer the barrier of cancer, and to study the mechanism of various disease and aging in life science. Laboratory animals also play a vital role in monitoring public hazards and pollution, protecting the environment for human's survival, and producing more and better farm products in proving human's daily life. Neither the import nor the export experimental animals are indispensable materials in pharmacy, biological products, pesticide, foodstuff, addictives, chemical products, cosmetics, aerospace, radioactive, and military products. Experimental animals always have safety evaluation and effect testing as human being's substitute. In the life science researches, the issue's establishment and achievement level are all decided by the quality of experimental animals. Without experimental animals, our scientific experiments, academic achievements, even papers cannot be recognized by international experts, some experts even look down upon on them or regard them as a heap of waste paper.

People established experimental animal science is to make the animal experiment more scientific. Laboratory animal science becomes an inalienable part of modern science and technology; it becomes a self-governed comprehensive fundamental science department. As an important means of science research, this science is important for the reason that it impact on the science achievement level directly. On the other hand, as a science, its improvement and development will take many new studies into new research field. Therefore, the importance of laboratory animal science technology can be summarized by the following sentences. Laboratory animal science is an important part of modern science and technology; it is the fundamental and requirement of life science; it is an important standard to measure a country or a scientific institution's standard.

II. Disquisitions on the Animal experiments and Laboratory Animal Science

The development of laboratory animal science produce many problems which bring human certain negative influence and various discussions.

2.1 Cruelty of Animal Experiment to Animal

Many animal experiments are cruel to animals. Here are two cases of notorious ruthless animal experiments.

2.1.2 the "Most Noxious" Test—Lethal Dose 50

The Lethal Dose 50 (LD50) is a standardized measure for expressing and comparing the toxicity of chemicals. The LD50 is the dose that kills half (50%) of the animals tested in 14 days. The test usually lasts for 3 months.

First, the researchers use a long tube to inject highly concentrated testing materials into animals' body. Generally, for the data accuracy reason, researchers do not provide anesthetic to animals. From the beginning of observation period 50% animals must be killed. After death of over 50% animals, the observation period is over. The survival animals will be killed or dissected.

To the experimental animals, this experiment put them live in pain and hopelessness. Before the death, animals are in a state of serious weak. They present diarrhea, cramps and congestion of their mouths, eyes, and rectums. Experience psychologist Richard Ryder have experienced the project in Oxford and Cambridge, he describes animal's suffering: Since most cosmetics are not obvious toxic, so a dog or a rabbit must be forced to drink unimaginable huge doses of this substances, thereby blocked or hurt their gut, or other physical behavior led to animal deaths. Even general food you will feel very uncomfortable when it force poured into your mouth. And now, the animals are facing to eat a mass of powder, cosmetic, and hair dye unwillingly, it must be more painful. It's dogmatically that in order to amend the LD50 test inject a huge dose of testing materials which enough to kill animals. Obviously, the death process itself tend to be extend and more miserable.^[1]

2.1.2 Terrible Draize test

The Draize Test is an acute toxicity test devised in 1944 by Food and Drug (FDA) toxicologists John H. Draize and Jacob M. Spines. It designs for testing the properties of cosmetic and daily products. According to the report, solutions of products are applied directly into rabbits' eyes. Clips are placed on the rabbits' eyelids to hold them open during the test period, during which time the rabbits are placed in restraining stocks. The researchers drop bleaching agent, shampoo or ink into the rabbit eyes. The animals are observed for up 14 days, for sign of redness, swelling, discharge, ulceration, hemorrhaging, cloudiness, or blindness in the tested eye. A researcher describes the most serious reaction, "Because of the cornea, or inner eye serious damage, animal completely blind. Animal rapid closed eyes, with bray, grasp eye, beating and strive to escape." [2]

^[1] Richard D. Ryder, Victim of Science: the Use of Animals in Research [M] London: Davis-Poyter, 1975 (36)

^[2] Journal of the Society of Cosmetic Chemists [J] 1962 13:9

Many tested materials can destroy the rabbit eyes, such as eyes deformation, iris fester, pupil ulcer, and cornea decay. To make matter worse, the experiment was not allowed to inject anesthetic to animal's body for accuracy reason. The data of United States Department of Agriculture shows that only in 1983 toxicological testing used 55,785 rabbits as well as chemical companies used the 22,034. Although there is no specific record reveals how many rabbits doing with Draize test, it must be an unimaginable number. [3]

2.2 The Difficulty of Animal Experiments Results' Appliance and the Adverse Consequence of Animal Experiment

Animal experiments results are not only difficult to adapt to humans, but also can produce adverse outcome. In order to prove this conclusion, we take animal toxicity test and various animals' psychology experiments to illustrate this issue.

2.2.1The Difficulty of Animal Experiments Results' Appliance on Human Beings

The toxicity experiments mentioned above caused a great agony to animals. It is not only difficult to apply to human body but also have the opposite effects.

This conclusion gained many experts and the doctor's approval. In Long Beach, California, Doctor Christopher Smith said, "This kind of experiment cannot predict the result after people exposure to toxicity, or guide poisoning treatment. As a 17-year-old professional emergency doctor, I haven't heard about emergency physicians dealing with accidents poisoning and contact poisons reference to Draize test with the eyes damage. I never turn to animal experiment results in my own treatment with accidental poisoning patients. Emergency physicians according to the case report, clinical experience, and "on-the-spot" experiences material to decide the best treatment for patients." [4]

Actually, animal experiments' conclusion for one species is often quite different from that for another. For example, treatment of leprosy had caused adverse reactions. Before it goes to the public, a lot of experiments had been done. Laboratory precedes a serious toxicity experiment on pregnant dogs, cats, rats, sulkies, and hens while some doubt it caused fetal abnormalities. The result shows that except for a special strain of rabbit produced fetus malformation, the others manifest offspring deformity.^[5]

10x1cology [M] 15(1):31-41, 1979

^[3] Toxicology [M] 15(1):31-41, 1979

^[4] Physicians Committee for Responsible Medicine (PCRM) PCRM News [J] Washington 1988(7-8), p.4

^[5] S.F. Paget Toxicological Method [M] Blackwell Scientific Publications 1970,pp.4 134-139

2.2.2 The "Already-known" and even "Boring" Conclusion

This kind of experiments usually weird and terrible, most of them study in many meaningless and trivial problems. It is obviously that the employ of animals do not have absolutely necessity.

Scholars of State University of New York at Oswego use male mice to observe the effect of castration to execution behavior. There are three groups of male mice in a cage, a group of castrated, a group of male hormone injected after castration, a group without castrated, and a one-day-born mouse also in the cage. The researcher records the rate of male mice kill and eats the baby. [6] In Tufts University, researchers study in attack behavior on monkeys, rats, and mice, they conclude that animals without alcohol have stronger attach intention than animals with alcohol. [7]

Harry F. Harlow, University of Wisconsin, processes an experiment so-called the "motherless mothers". Harlow devised a serious of ingenious studies in which infant monkeys were raised in cages without their natural mothers, or with surrogate "mother" instead. The surrogate "mothers" did not nurse, comfort or protect their young, nor did they harm them. Harlow's research suggested that not only does the child look to his mother for basic needs, but he also needs to feel love from the caregiver. His findings show some long-term psychological physical effect of delinquent or inadequate attentiveness to child needs and the importance of mother/child bonding.^[8]

The experiments' conclusions discussed above are fully demonstrate that the experimental psychologists do great efforts to tell us the results we've already knew in scientific terms. As long as observe slightly attentively, we can get the same conclusions without harm to animals. [9]

2.3 The Motivation of Animal Experiment

Many people set goals of gaining fame through animal experiments. Some students make animal experiments for degree, some scientific researchers for personal fame and wealth. When freshmen of medical school, biological college, and veterinary medicine college

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^[6] Kenneth M Rosenberg, "Effects of Pre-and Post pubertal Castrain and Testerone on Pup-Killing Behavior in the Make Rat", 13 Physiology & Behavior

^[7] Klaus A Miczek, James T. Winslow, and Joseph F. De-Bold, "Heightened Aggressive Behavior by Animals Interacting with Alcohol-Treated Conspecifics: Studies with Mice, Rats, and Squirrel Monkeys," 20(3) Pharmacology Biochemistry & Behavior 349 (1984)

^[8] Murry J. Cohen, A Critique of Materal Deprivation Monkeys Experiments at the State University of New York Health Science Center [M] (New York: Medical Research Modernization Committee, 1996)

^[9] Peter Singer Animal Liberation [M] Shangdong: Qingdao Press 2004,9:45

entering university, their professional courses contain live animals dissection definitely. As a graduation needs, it is impossible to refuse this teaching course, unless they want to convert professions or drop out of school. If they want to continue learning, or get further education in Mastership, their professors will keep them doing animal experiments. Naturally, when they have academic success and become some one's tutor, they will following in the footsteps of their professors to let their students involved in animal experiments.

As to the animal experiment research projects, people always concerned about position promotion, bonus, and research funds, something related to materials. There is no dispute that animal experiment projects do really help to solve practical problems. In fact, the reverse is probably true. Similar to the liberal arts academic corruptions, many animal research projects have studied previously, or already being solved. The issues which have not been studied are too hard. Such animal experiments were mostly in some nonsense issues. In some how, it is always "new", or "a little bit" progress which also can give material benefits in return.

This situation was recognized by the researchers themselves. For example, Professor Harlow, the holder of "motherless mother" experiment mentioned earlier. He served for *Journal of Comparative and Physiological Psychology* as an editor for 12 years. Harlow estimates that he had judged more than 2,500 manuscripts, "most of the experiments are not worthwhile as well as the data meaningless to publishing," he said.^[10]

It follows that animal experiments become a ladder of researcher's academic success, paper publishing, and reputation improvement. Compared with the liberal arts corruption, animal experiments at the cost of unprovoked pain and life destruction to innocent animals whereas liberal arts corruption defiled researcher's reputation and waste of a few pieces of writing paper.

2.4 The Lack of Unified and International Accepted Standards in Laboratory Animal Research Field

We don't have a unified and international accepted standard in experimental animal field. The fact is each country has its own standard. Even in a country, each district has different criterion. For example, in China, we do not pay much attention to experimental animals, which brings out many painful lessons. For the lack of proper and qualified animal in swine fever vaccine manufacturing, a great deal of vaccinated pigs died and epidemic disease spread in Inner Mongolia, Shaanxi, Sichuan, Hebei, Henan, Hubei, Guangdong recent years

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^[10] Journal of Comparative and Physiological Psychology[J] 55:896,1962

continuously, which brings about great damage and the adverse political impact. In biological products working, export of the measles vaccine for man and the Marek's disease vaccine for livestock have been affected without SPF(Specific Pathogen Free)-chicken and chicken pollution leuoviruses. Due to the complex species, difficulties in quality maintain, strict on specifications, less time service, uncontrolled the reproductive rules, and a high dependence on living environment characteristics, these all decides experimental animals' production is harder than other industrial products. It is often causing special difficulties in manufacture and circulation. It needs hard effort to adopt internationally recognized experimental animals standards to do science research in China.

III. The Legislation of Experimental Animals in Europe and China

To solve the problems generated in animal experiments, many countries have adopted legislative measures to regulate the animal experiments behavior.

3.1 European Convention an Experimental Animal Legislation in European Countries

European laboratory animal welfare act aims at reducing sufferings of laboratory animals, approval experiment projects, information report, and so on.

For the purpose of experimental animals, *On the Protection of Animals Used for Scientific Purpose European Convention* (2010/63/EU), Article 5 rules about experimental purposes strictly: (1) The avoid, prevention, diagnosis or treatment of disease, ill-health or other abnormality or their effects in human being, animals or plants. (2) The assessment, detection, regulation or modification of physiological conditions in human beings, animals or plants. (3) Protection of the natural environment in the interests of health or welfare of human beings and animals.(4)Basic research (5) Higher education, or training for the acquisition maintenance or improvement of vocational skills. (6) Forensic inquires.

To minimize the pain of animals, *On the Protection of Animals Used for Scientific Purpose European Convention* (2010/63/EU) article 13 points out that in choosing between procedures, those which to the greatest extent meet the following requirements shall be selected (a) use the minimum number of animals (b) involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm (c) cause the least pain, suffering, distress or lasting harm." Article 14 claims Member States shall ensure that, unless it is inappropriate, procedures are carried out under general or local anesthesia, and that analgesia or another appropriate method is used to ensure that pain, suffering and distress are kept to a minimum. Procedures that involve serious injures that may cause severe pain shall not be

carried our without anesthesia. In addition, The Kingdom of Belgium published *Concerning* the Protection of Animal Welfare Laws (1986 August, 4th), and German, Animal Welfare Act (1998 revision), also have similar regulations.

In the inspections and reporting section, On the Protection of Animals Used for Scientific Purpose European Convention (2010/63/EU) Article 5 says clearly that the experiments applied to higher education or training for the acquisition. According to Article 54, Member States shall collect and make publicly available on an annual basis, statistical information on the use of animals in procedures, including information on the actual severity of the procedures and on the origin and species of non-human primate used in procedures. Member States shall submit that statistical information to the Commission. German Animal Welfare Act (1998 revision) Article 7 regulates experiments causing lasting or repeated severe pain or suffering to vertebrates may be carried out only if the results are expected to be of outstanding importance for the fundamental needs of human beings or animals, including the solution of scientific problems. Britain's Animals (Scientific Procedures) Act (1986) has strict regulation on qualification of experimenter. The person who takes animal experiments should have the personal license. A personal license is a license granted by the Secretary of State qualifying the holder to apply specified regulated procedures to animals of specified descriptions at a specified place or specified places. In Britain, no personal license shall be granted to a person under the age of eighteen. These rules help to prevent those trivial animal experiments recurring to animals; they also reduce a lot of unnecessary pain and suffering.

Finally, in some absolutely forbidden experimental projects, the European Union and the European countries also have rigid regulation. *On the Approximation of the Laws of the Member States Relating to Cosmetic Products* (2009/1223/EC) Article 4 paragraph 1 writes about Member States prohibit the marketing of laboratory animal cosmetic products, the dead line is 2004, March 11th. The Dutch's *Experiments on Animals Act* (1997), Article 10 regulates no animal experiment shall be conducted for the purpose of developing new or testing existing cosmetics covered by rules based on the *Commodities Act*. German *Animal Welfare Act* (1998) Article 7, experiments on animals to develop or test weapons, ammunition and related equipment shall be prohibited. In principle, experiments on animals to develop tobacco products, detergents and cosmetics shall be prohibited.

In addition, the experiment information reporting system is also a guarantee that animal experiment supervised by the general public. And it also leads right direction of animal experiments development and brings lots of benefits to the public. For example, *On the Protection of Animals Used for Scientific Purpose European Convention* (2010/63/EU)

Article 54 rules out Member States shall collect and make publicly available. For some trivial purposes experiments, or some unnecessary projects for human beings, European countries also have rigid forbidden as we mentioned before.

3.2 Legislation of the Chinese Lab Animal Adimistration

Compared with farm animals, the lab animals' welfare in China shows a better situation because some of the advanced practice reference with the international laws and principles. The Guideline on the Humane Treatment of Laboratory Animals (2006) is the country's first broad animal welfare regulation. The protections of animals' are a particular focus of the guidelines, which call for adherence to the 3Rs—replacement, reduction, and refinement. Furthermore, the Statute on the Administration of Laboratory Animals (1988), approved by China's State Council, is the highest policy and regulates every aspect of lab animal procedures for experimental and other scientific purposes. Such as, lab stuff must get regular medical checkups, receive training and obtain a personal license before handling animals, and take care of the animals in a humane manner. Behaviors such as abuse or teasing of lab animals are prohibited and subject to punitive measures. In alternative methods, pain management, and maltreat on experimental animals, China does a good job.

Concerned on the animal experiments purpose inspection, in the comparison of China's animal welfare and advanced foreign animal welfare, we find many disparities. For experimental purposes inspections, Chinese relevant laws and regulations are:(1) Regulations for the Administration of Affairs Concerning Experimental Animals (1988) requires institutions shall submit scientific research topic and scientific research achievements; all animal experiments must use qualified and certified lab animals as the basic conditions (2) Regulation on the Management of Lab Animal Quality Control (1997)sets a national unified licensing system for lab animal, it rules out details requirements and procedures for licenses application, review, and approval and for facility inspection and supervision. The similar regulation also can be seen in the Regulation on the Management of Lab Animal Licensing System (2002). China's animal experiments inspection system only focuses on the quality and source of experimental animals as well as lab's hardware facilities. When the problem goes to animal experiments' purposes, we can't find related regulations. In pursuing fame and fortune, some institutions and individuals proceed trivial purposes experiments or experiments which we have had conclusion, it will leads animals experience unnecessary pain and suffering again. What is more important, if such situation continues, the state allocate funds and personal tax continue to support this kind of non-progressive scientific research, this will bring scientific research into academic corruption, and animals in this process manages to be the victim of human's vanity.

IV. Improvement of Experimental Animal Welfare and Enforcement

Despite countries around world have adopted legislative measures to regulate the behavior of animal experiments, but in the process of legislation and enforcement is not satisfactory in many places. We still have a long way to go.

We should be in line with "take reasonable and painless" to lab animals, and try our best to minimize the pain and suffering to animals which use in experiments. Firstly, we should consummate experiment inspection system, do animal experiments with a purpose. Secondly, after determining the need of animal experiment, we had better look after for alternatives. If we have to put animal into process, we need to do our best to minimize or prevent the suffering. After an experiment, animals should be euthanized according to humane endpoint principles.

Regardless of the lives of animals, some people only trace for research funding, school entrance, commercial interests, they set fame and wealth as goal, and they did nothing to help the development of lab animal science. Such corrupt customs not only in China, but also exists in foreign countries. Therefore, improving animal experiments inspection system is playing a key role to ensure animal welfare. So, the animal protection law recommendation of China proposed to build a laboratory animal ethics review committee for the purpose of the experiment, the expectation of benefits, and the harm of animals, a comprehensive assessment of death, to ban meaningless breeding, abuse, and killing.^[11]

For those inspection-passed experiment projects, the object of experiment should find alternatives as far as possible. The principle was first introduced by Britain zoologist Russell and microbiologist Burch, 1959. Replacement: the use of non-animal methods such as cell cultures, human volunteers and computer modeling instead of animals to achieve a scientific aim. Such regulations can be seen in *Chinese Guidelines on the Humane Treatment of Lab Animals*.

For those experiments which need to use animals, we should follow the principle of painless. Specifically, when using anesthetic does not affect the experiment results, the experimenter must give animal anesthetic. In this circumstance, we can make sure that experiments carried our normally meanwhile animals do not pain.

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^[11] Sun jiang, He li, Liang Zhibo, A study of Prevention of Cruelty to Animals by Legislation, [M]Beijing: China University of Political Science and Law Press

At the end of experiment, we shall not put the same animal into another experiment, for example, a mouse cannot be re-used in another experiment. Let us think about it, animal's sacrifice in the interests of human, its body and mind has been greatly hurt and pain. So from a humanitarian perspective, we should have the obligation to prevent it repeatedly suffer from experimental pain.

Finally, in the end of experiment, laboratory staffs should try their best to help animal recover from experiment. The animals who cannot recover from experiment or facing survival dangerous, humane method of execution should be taken. *Appendix A : Of the European Convention for the Protection of Vertebrate Animals Used for Experimental and other Scientific Purpose* (2006) regulates humane killing. All humane methods of killing animals require expertise, which can only be attained by appropriate training. Animals should be killed using a method that adheres to the principles set by the *European Commission Recommendations for the Euthanasia of Experimental Animals*.

The reform of experimental animal welfare act mentioned above can be seen in Chinese lab animal laws, but how to ensure the enforcement could be a problem. Because many animals' initiatives treatments are meant to increase testing costs, laboratory staff may neglect of the basic interests of animals for financial savings. On this point of view, the author proposed to establish the opinion that basic interests of animals is more important than the interests of human's trivial idea. Since animals have made tremendous sacrifices in the interests of human, all human have to do is spend more money and more time to meet the animals' very basic and important needs. As the only moral spokesmen on the planet, we should take such obligations.

References

- [1] Richard D. Ryder, Victim of Science: the Use of Animals in Research [M] London: Davis-Poyter, 1975 (36)
- [2] Toxicology [M] 15(1):31-41, 1979
- [3] S.F. Paget Toxicological Method [M] Blackwell Scientific Publications 1970,pp.4 134-139
- [4] Kenneth M Rosenberg, "Effects of Pre-and Post pubertal Castrain and Testerone on Pup-Killing Behavior in the Make Rat", 13 Physiology & Behavior Biochemistry & Behavior [M]349 (1984)

- [5] Murry J. Cohen, A Critique of Materal Deprivation Monkeys Experiments at the State University of New York Health Science Center [M] (New York: Medical Research Modernization Committee, 1996)
- [6] Peter Singer Animal Liberation [M] Shangdong: Qingdao Press 2004,9:45
- [7] Sun jiang, He li, Liang Zhibo, A study of Prevention of Cruelty to Animals by Legislation,
- [M] Beijing: China University of Political Science and Law Press
- [8] Journal of the Society of Cosmetic Chemists [J] 1962 13:9
- [9] Physicians Committee for Responsible Medicine (PCRM) PCRM News [J] Washington 1988(7-8), p.4
- [10] Journal of Comparative and Physiological Psychology [J]55:896,1962
- [11] Klaus A Miczek, James T. Winslow, and Joseph F. De-Bold, "Heightened Aggressive Behavior by Animals Interacting with Alcohol-Treated Conspecifics: Studies with Mice, Rats, and Squirrel Monkeys," 20(3) Pharmacology

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