Animal Testing And Non-Animal Alternative Testing Global Market Opportunities And Strategies To 2035

The Business Research Company

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Executive Summary

This report describes and evaluates the animal testing and non-animal alternative testing market in major geographies.

Animal testing or experiment on animals done in the early stages of drug development and for toxicity and safety assessment of medical devices, chemicals, pesticides, cosmetics, and food compounds. Animal experiments are necessary before testing on humans mainly to evaluate toxicity, pharmacokinetics, and safety of a drug or a chemical. However, there is an increasing pressure from the animal welfare organizations on governmental agencies and companies to use non-animal alternative testing technologies. These technologies include in-vitro cell and tissue cultures, organ-on-chip, computer simulations, 3D bio printing of tissues, and synthetic skin substitutes, among others. Industries such as pharmaceuticals, medical devices, chemicals & pesticides and food are increasingly adopting these technologies to replace animal testing.

Animal Testing

The global animal testing market was valued at $10.74 billion in 2019 and the market is expected to grow at a compound annual growth rate (CAGR) of 4.27% during 2019-2025 and at a CAGR of 2.46% during 2025-2035. USA and Japan are the major animal testing markets in the world. The USA's animal testing market was valued at $4.67 billion in 2019, and is expected to grow at a CAGR of 1.49% during 2019-2025 and at a CAGR of 0.57% during 2025-2035. Japan's animal testing market was valued at $1.03 billion in 2019. The market is forecast to grow at a CAGR of 3.51% during 2019-2025, and at a CAGR of 1.73% during 2025-2035.

Non-Animal Testing

The global non-animal alternative testing market was valued at $1.110 billion in 2019. The market is expected to grow at a CAGR of 10.40% during 2019-2025. The USA's non-animal alternative testing technology market was valued at $0.336 billion in 2019. The USA's market is forecast to grow at a CAGR of 11.99% through 2025. Japan's non-animal alternative testing technology market was valued at $0.058 billion in 2019 and the market is forecast to grow at a CAGR of 6.79% through 2025.

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Introduction And Market Characteristics

This global market report covers the following time frames:

- 2019: historic period
- 2020 – 2035: forecast period

The report evaluates the market across regions and the major economies within each region.

The geographic regions used for the market analysis are as follows

Figure 1: Geographic Regions Covered

Summary

Data Type	Global	Regions
Forecast (2020-2035)	✓	✓
Segmentation By End-Use Industry		✓

Market Definition

The animal testing market consists of the total expenses incurred by end-use entities that use animals for testing their products. End-use entities include academic research institutions and various industries (such as pharmaceuticals, medical devices, chemicals & pesticides and cosmetics,) that conduct animal testing during product development. Pharmaceutical and medical device companies also use animal testing to understand basic disease mechanisms. End-use entities may also outsource these tests to clinical research organizations (CROs). The animal testing market covered in this report includes sales of animal testing services by CROs to end use industries.

The market includes the costs of animal models and the costs of animal testing operations (such as animal maintenance and feed) during drug/ product testing. This market does not include animals caged in companies as stock and not used for testing, and animals used for breeding.

The market takes into account the testing performed on animals in a particular geography i.e. where the testing happens, irrespective of where the products (drug or chemicals) that need to be tested are produced.

The non-animal alternative testing market is the total expenses incurred by end-use entities that use alternative technologies instead of animals for testing their products. End-use entities include academic research institutions, and various industries (such as pharmaceuticals, medical devices, chemicals & pesticides and cosmetics) performing animal testing to conduct basic

research, toxicology profiling, and others. The non-animal testing market covered in this report includes sales of non-animal testing services by CROs to end use industries. The market is inclusive of the costs of alternate technology tools and other operational costs involved in using these tools for various preclinical testing purposes. The market takes into account the testing performed in alternative technologies in a particular geography i.e. where the testing happens, irrespective of where the products (drug or chemicals) that need to be tested are produced.

Animal Testing

Animal testing or in-vivo testing is the use of living animals in scientific experiments to assess the safety and effectiveness of new products developed in the biopharma, medical devices, chemicals, food, and other industries. Animal testing allows scientists to understand the information about how the human body might react to specific substances. The study on animals is a vital part of the research because the basic cell process and physiology of animals is similar to that of humans.[i]

Animal testing is performed during preclinical stages[ii] of drug discovery or for toxicity testing of chemicals, pesticides and other food products. These preclinical studies are important to evaluate preliminary efficacy, toxicity, pharmacokinetics, and safety information of a drug or chemical before testing on humans.[iii] Academic research organizations, biopharmaceuticals companies, cosmetics companies are some of the organizations which conduct experiments on animals. Animals including mice, rats, rabbits, hamsters, and guinea pigs are commonly used for animal testing. [iv, v] Non-human primates including chimpanzees, horses, and monkeys are used for specific studies in the biopharmaceutical industry.

Toxicity tests conducted for a drug during preclinical studies include acute dermal systemic toxicity, acute inhalation toxicity, acute oral systemic toxicity, dermal corrosivity and irritation, dermal phototoxicity, developmental and reproductive toxicity, genetic toxicity, skin sensitization, and others.

In the USA and in Japan, animal testing end-use companies have adopted 3R principles to reduce, replace, and refine animals used in laboratory research. The 3R principle states that non-animal testing methods should be adopted wherever appropriate to replace animal experiments. It also states that the companies using animal models should make every effort to reduce the number of animals used in each study, and to minimize the potential for pain and distress toward animals.

Non-Animal Alternative Testing

Non-animal alternative testing technologies include those technologies such as in-vitro cell and tissue cultures, organs-on-chips (OOCs), computer simulations, 3D bioprinting of tissues, and synthetic skin substitutes.[vi] These technologies replace animal testing in end-use industries including pharmaceuticals, medical devices, chemicals & pesticides, food, and others.

Non-animal alternatives testing/animal replacement can be simply defined as any scientific method employing non-sentient material which may replace the use of conscious living vertebrates in animal experimentation.[vii]

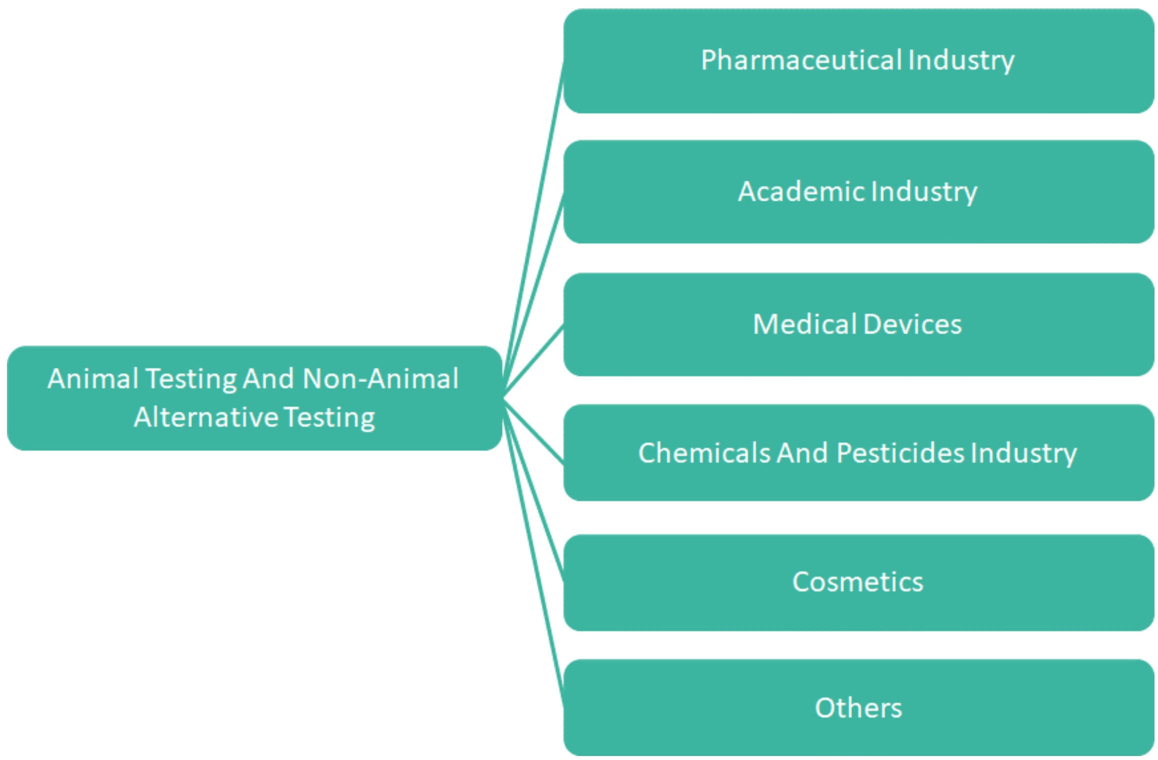
Non-animal methods are not hindered by species' differences that make applying animal test results to humans difficult or impossible. They also usually take less time to complete and are better able to predict how chemicals will react in the human body.[viii][ix]

Interest in non-animal alternative testing technologies has been growing, as they are cost-effective, more efficient, and often less time-consuming. Protests by animal welfare organizations such as People For The Ethical Treatment Of Animals (PETA) and Cruelty-Free International, have put tremendous pressure on both federal agencies, and companies (that perform animal testing) to reduce or eliminate animal testing and to use alternative non-animal testing methods wherever applicable.[x] Owing to these factors, the EU has banned animal testing in the cosmetic industry, while the USA does not mandate any animal testing for cosmetic products. In the USA, the environmental protection agency (EPA) has decided to end the use of animal testing in the chemical industry by 2035,[xi] whereas National Institutes of Health (NIH) and other regulatory agencies have implemented proposals to support alternative non-animal testing technologies for both the pharmaceutical and medical device industries.[xii]

Animal Testing And Non-Animal Alternative Testing Market Segmentation By End-Use Industry

The animal testing and non-animal alternative testing market is segmented by end-use industry in pharmaceuticals, academic research, medical devices, chemical and pesticides, cosmetics and others.

Figure 2: Global Animal Testing And Non-Animal Alternative Testing Market Segmentation By End User Industry



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Sources: TBRC Analysis

Pharmaceutical Industry

The pharmaceutical industry market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used for testing pharmaceutical drugs. Animal techniques are used to test for attributes such as absorption, duration of action and delivery to the target, and safety tests are performed on animals, prior to clinical trials in humans, in order to select the most suitable lead chemical and dosage form for drug development[xiii].

Academic Industry

The academic industry market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used for animal study and research. Animals testing in academic institutions is used for research, education and include animals used in experiments at science fairs, in after-school science clubs, and in 4-H projects, among other animal-related science projects and other uses.[xiv]

Medical Devices

The medical devices market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used for testing the safety of medical devices, test their potential performance when used in a living system, and the biologic response that a living system may mount towards the device[xv]. Medical devices such as cardiac valves, stents and others, before they are introduced in human clinical trials is required for both ethical and legal reasons.[xvi]

Chemicals And Pesticides Industry

The chemicals and pesticides industry market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used for testing in the chemicals and pesticides industry. Animal testing is used in the chemical industry for chemical safety assessment of industrial chemicals, chemicals in consumer products, pesticides, and biocides.[xvii] Animal-poisoning tests is done in pesticides industry to assess the safety of a single new pesticide to market.[xviii]

Cosmetics

The cosmetics market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used for testing cosmetics products. Animal testing is used in cosmetics industry to assess the safety of new ingredients and test hypoallergenic properties of cosmetic products for use by humans.[xix]

Others

The others market in the animal testing market consists of sales of animal testing services by entities (organizations, sole traders, and partnerships) that are used in other industries such as diagnostics, household products, food & beverage industry and other industries.

Cost Analysis For Animal Testing And Alternative Technologies

This section provides cost analysis for animal testing and non-animal alternative testing methods. It includes the average cost of animal species such as mice, rats, rabbits, guinea pigs, and non-human primates, and the cost of non-animal alternative testing methods accepted by OECD TG guidelines. This section also covers comparative cost information for animal testing and alternative methods to understand the cost-effectiveness and time efficiency of alternative methods.

Average Cost Of Laboratory Animals

The table below shows the average cost of animals used in laboratory research:

Table 1: Estimated Average Cost Of Animals, 2020 ($)

S.No	Animal Species	Type	Average Price ($)
1	**Rats**	Outbred	$40
		Inbred	$70
		Disease/Translational Rats	$220
2	**Mice**	Outbred	$20
		Inbred	$70
		Hybrid	$35
		Immunodeficient Model	$130
3	**Guinea Pigs**	-	$250
4	**Rabbit**	-	$270
5	**Hamsters**	-	$60
6	**Non-Human Primates**	-	$6000

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Source: NAVS[xx,xxi,xxii] Charles River Lab[xxiii]

Laboratory animals such as mice, rats, guinea pigs, rabbits and non-human primates (monkeys) are widely used for scientific and research purposes. In the USA and Japan, mice and rats are most commonly used for laboratory experiments, which account for more than 96% of the total animal species used.[xxiv] The average cost of outbred and inbred rats is $40 and $60 respectively. The inbred rat strains are most widely used over outbred strains, due to their uniformly defined genetics that provides feasibility to use a lesser number of animals to detect a specified response in laboratory experiments.[xxv] The average price of disease/translational rats is $220. Translational rats are used to develop disease models in translational research such as trauma rat models using brown rats.[xxvi]

The average prices of mice strains such as outbred, inbred and hybrid are $20, $70, and $35 respectively. Immunodeficient mouse models are very useful for immunology, infectious disease, cancer, stem cell biology, and other research studies. The development and use of an increasing number and variety of genetically engineered immunodeficient mouse models have been vital for understanding the gene-driven cellular and molecular mechanisms and pathophysiological manifestations of immune disorders that are similar to mice and humans. The average price of the immunodeficient mouse model is $130. The mice and rats were widely used for preclinical toxicology studies.

The average cost of a guinea pig is $250. These are used in infectious disease research, including studies for tuberculosis and diphtheria. They are also used to study safety tests and toxicity studies in other research areas such as allergy, respiratory, and auditory systems.[xxvii]

New Zealand White rabbits, large albino rabbits are the most common breeds of rabbits used in research to study the safety and toxicity of substances such as drugs, chemicals, and medical devices. The average cost of New Zealand white rabbits at Charles River Laboratories is $270 depending on age and weight.[xxviii] Hamsters are the most commonly used animals for behavioral research studies. The Syrian (golden) Hamster average price is $60. Hamsters are also used in cancer and infectious disease research due to their short life cycle and susceptibility to many pathogens.[xxix]

Non-human primates such as cynomolgus macaques, rhesus macaques, African green monkeys, squirrel monkeys, and baboons are used in biomedical and behavioral research. The average price of a monkey is $6000.[xxx]

Average Cost Of Non-Animal Alternative Testing Methods

The cost of non-animal alternative testing technologies is much lower compared to traditional animal testing. According to a study 'Impact of organ-on-chip technology on pharmaceutical R&D costs' published in drug discovery today journal, it has estimated that organ-on-chip technology can reduce the cost of pre-clinical testing by 73%, and increase the rate of success (during preclinical drug discovery stage) by 80%. In addition to cost and success rate, organ-on-chip technology can save 40% of the time during the pre-clinical stage compared to animal testing.[xxxi]

Emulate, a non-animal alternative testing technology company sells its system close to $100,000 and a pack of 24-chips is around $10,000. CN Bio Innovations also works on a human body-on-a-chip. The company sells a liver-on-a-chip, with prices for the liver chip at $22,000. This technology is faster and more cost-effective than animal research.[xxxii] iPS cell lines are also used as non-animal testing methods during research and development of new drugs. For instance, the average cost to produce iPS cell lines is around $15,000.[xxxiii]

Adoption of 3R's In Europe

The principle of the "Three Rs" has been present in the European Union (EU) legislation in spirit, from as early as 1986, when the first EU legislation for the protection of animals used for experimental and other scientific purposes was adopted. However, Directive 2010/63/EU on the protection of animals used for scientific purposes, for the first time in EU legislation spells out the principle of the "Three Rs" and makes it a firm legal requirement. The principles of Replacement, Reduction and Refinement must be considered systematically at all times when animals are used for scientific purposes in the EU. Under the Directive, the term "scientific purposes" covers all uses of animals for the purposes of basic, translation and applied research, regulatory testing and production as well as for the purposes of education and training.

The term 'alternatives' in this context includes all assays, tests, methods, techniques, tools, strategies and approaches etc. that contribute to the practical implementation of the "Three Rs". That is

- To obtain the required information without the use of live animals;
- To reduce the numbers of animals whilst obtaining the same level of information;
- To refine the use of live animals so as to cause less pain, distress or suffering, or improve the welfare of the animals.

Alternative approaches provide opportunities to advance the "Three Rs", but equally aim at developing better and more predictive scientific tools to protect human and animal health and the environment.[xxxiv]

Some of the obligations to the Member States (Belgium, Bulgaria, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Latvia, Lithuania, Slovakia, Slovenia, Sweden and United Kingdom) to facilitate increased uptake of alternative approaches in Article 47 of the Directive:

- The Commission and the Member States shall contribute to the development and validation of alternative approaches which do not involve the use of animals or use fewer animals or which entail less painful procedures, and they shall take such other steps, as they consider appropriate to encourage research in this field.
- Member States shall assist the Commission in identifying and nominating suitable specialized and qualified laboratories to carry out such validation studies.
- Member States shall, at national level, ensure the promotion of alternative approaches and the dissemination of information thereon.
- Member States shall nominate a single point of contact to provide advice on the regulatory relevance and suitability of alternative approaches proposed for validation.[xxxv]

Directive 2010/63/EU established the European Union Reference Laboratory for alternatives to animal testing, EURL ECVAM, and describes as one of its key tasks the co-ordination of formal validation studies at EU level to facilitate rapid uptake of new methods and approaches to replace reliance on animal testing.[xxxvi]

EURL ECVAM has contributed to the validation of the test methods listed below:

Table 2: Non-Animal Alternative Testing Methods Accepted By The European Commission

S.No	Toxicity Area	Method	Regulatory Acceptance
1	Acute oral toxicity	Fixed Dose Procedure	OECD test guideline 420
2	Acute oral toxicity	Acute toxic class method	OECD test guideline 423
3	Acute oral toxicity	Up-and-down procedure	OECD test guideline 425
4	Acute dermal toxicity	-	OECD test guideline 402
5	Acute inhalation toxicity	-	OECD test guideline 403
6	Acute inhalation toxicity	Acute toxic class method	OECD test guideline 436
7	Acute inhalation toxicity	fixed concentration procedure	OECD test guideline 433
8	Acute fish toxicity	Fish acute toxicity	OECD test guideline 203 / EU test method C.1
9	Acute fish toxicity	Threshold approach for acute fish toxicity	OECD guidance document GD 126
10	Acute fish toxicity	Fish embryo acute toxicity test	OECD test guideline 236
11	Chronic fish toxicity	Fish early-life stage toxicity	OECD test guideline 210
12	Chronic fish toxicity	Fish short-term toxicity test on embryo and sac-fry stages	OECD test guideline 212 / EU test method C.15
13	Chronic fish toxicity	Fish juvenile growth	OECD test guideline 215 / EU test method C.14
14	Eye Irritation	The Cytosensor Microphysiometer (CM) toxicity test	OECD test guideline 405, the United Nations Globally Harmonised System (UN GHS), and EU Directive 1272/2008
15	Genotoxicity	Micronucleus Test (MNT)	The in vitro MNT has gained widespread international regulatory acceptance (OECD Test Guideline 487)
16	Phototoxicity	3T3 Neutral Red Uptake (NRU) Phototoxicity test	the method has been adopted as OECD test guideline No 432.
17	Skin Corrosion	Rat Transcutaneous Electrical Resistance (TER) test	OECD TG 430
18	Skin Corrosion	EpiSkin Skin Corrosion Test (SCT)	OECD TG 431

19	Skin Corrosion	EpiDerm Skin Corrosion Test (SCT)	OECD TG 431
20	Skin Corrosion	SkinEthic Skin Corrosion Test (SCT)	OECD TG 431
21	Skin Corrosion	EpiCS Skin Corrosion Test (SCT)	OECD TG 435
22	Skin Irritation	EpiSkin Skin Irritation Test (SIT)	OECD test guideline 439
23	Skin Irritation	EpiDerm Skin Irritation Test (SIT)	OECD test guideline 439
24	Skin Irritation	SkinEthic Skin Irritation test (SIT)	OECD test guideline 439
25	Skin Irritation	EpiCS Skin Irritation Test (SIT)	Validated by EURL ECVAM, Regulatory acceptance yet to be confirmed
26	Skin Sensitization	Direct Peptide Reactivity Assay (DPRA)	OECD TG 442C
27	Skin Sensitization	ARE-Nrf2 Luciferase Test Method: KeratinoSens	OECD TG 442D
28	Skin Sensitization	Human Cell Line Activation Test (h-CLAT)	OECD TG 442E
29	Skin Sensitization	U937 cell line activation test (U-SENS)	OECD TG 442E
30	Skin Sensitization	Interleukin-8 Reporter Gene Assay (IL-8 Luc assay)	OECD TG 442E
31	Toxicokinetic	Dermal absorption in vitro (ADME in vitro procedure)	(OECD TG 428, 2004)

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Source: European Commission[xxxvii]

Internationally there are more than 50 different alternative methods and testing strategies for animal testing which are validated and/or accepted by international regulatory authorities.[xxxviii] In the Europe, there are 31 alternative methods (as listed in the above table) with either regulatory acceptance or endorsement, with a view to replace, reduce, and refine animal use. Most of these tests are adopted from OECD test guidelines.

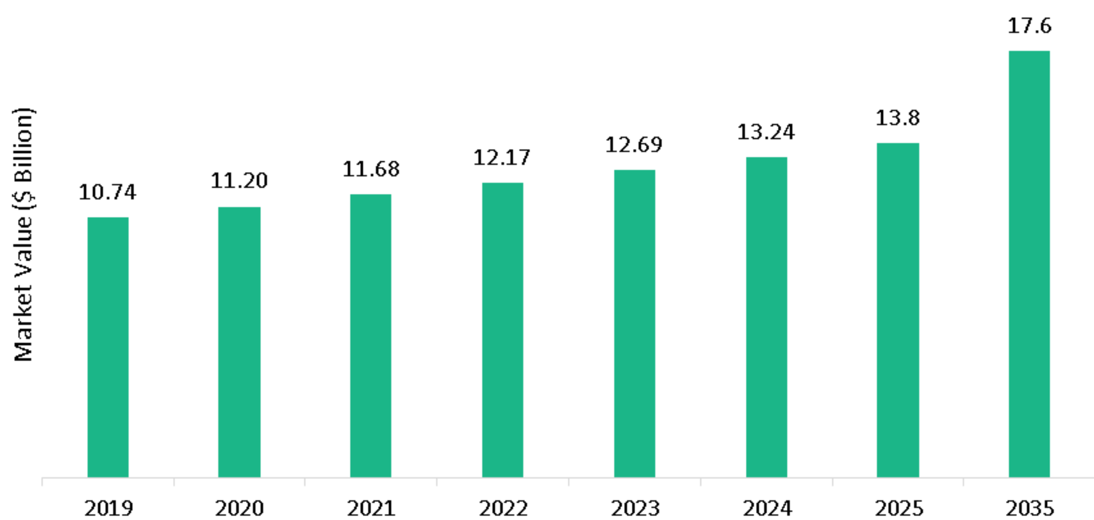
Global Market Size and Growth

Global Animal Testing Market Size And Growth

Global Animal Testing Market Value ($ Billion)

The chart and table below show the year-on-year growth of the global animal testing market during 2019 – 2035.

Figure 3: Global Animal Testing Market Size, 2019 – 2035, $ Billion



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Sources: National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary

Table 3: Global Animal Testing Market Size, 2019– 2035, $ Billion

Market	2019	2020	2021	2022	2023	2024	2025	2035	CAGR (2019-2025)	CAGR (2025-2035)
Animal Testing	10.74	11.20	11.68	12.17	12.69	13.24	13.80	17.60	4.27%	2.46%

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Sources: National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary

The global animal testing market is expected to grow from $10.74 billion in 2019 to $13.8 billion in 2025 at a compound annual growth rate (CAGR) of 4.27% and to $17.60 billion in 2035 at a compound annual growth rate (CAGR) of 2.46%.

The growth in the market is mainly due to increasing research & development activities in the pharmaceutical, medical device, and chemical industries and government regulations mandating animal testing for product approvals. [xxxix, xl, xli] In addition to that, regulatory mandate on animal testing across biopharma and chemical industries, increasing funding and grants for research, and adoption of in vivo toxicology tests by end-use companies will fuel the growth of the global market.

"The global animal testing market can be around $10-12 billion considering the fact that there are millions of rodent models being used across various industries. However, in the USA I believe the animal testing market growth will be slow."

- Chief Scientific Officer, In-Silico Biosciences Inc., USA

"The global animal testing market is around $8-10 billion currently with the US constituting 45% of the market. I think the USA market could only slow down, because if the industry (R&D of biopharma) think they have to do animal testing, then it has to be done."

- Business Development Officer, Emulate Bio, USA

Global Animal Testing Market, By Volume (Million Units)

The chart and table below show the year-on-year growth of the global animal testing market in terms of volume, during 2019 – 2035.

Figure 4: Global Animal Testing Market, Volume, 2019 – 2035, Million Units

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Sources: National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary

Table 4: Global Animal Testing Market, Volume, 2019– 2035, Million Units

Market	2019	2020	2021	2022	2023	2024	2025	2035	CAGR (2019-2025)	CAGR (2025-2035)
Animal Testing	101.35	104.60	107.96	111.43	115.00	118.69	122.50	149.30	3.21%	2.00%

The Business Research Company
Sources: National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary

The global animal testing market by volume is expected to grow from 101.35 million units in 2019 to 122.50 million units in 2025 at a compound annual growth rate (CAGR) of 3.21% and to 149.30 million units in 2035 at a compound annual growth rate (CAGR) of 2.00%.

The market growth (number of animals used in research) can be attributed to increasing funding and grants for basic research, to elucidate new disease mechanisms, regulatory mandate to conduct animal testing for safety and toxicology studies, and increasing research and development activities across the end-use industries including pharmaceuticals, medical devices, chemicals, and others.

TBRC estimates that the global animal testing market growth will slow down post 2025, as regulatory agencies will increasingly enforce the adoption of non-animal alternative testing technologies. Alternative technologies are likely to be preferred over animal testing methods owing to their low costs, high reliability, and ease of use. The number of animals used in research will reduce post 2025, which can be attributed to the US EPA's decision to end animal testing for chemicals in the USA and the FDA's road map for alternative technologies to replace animal testing. Regulatory guidelines by 'registration, evaluation, authorisation and restriction of chemicals (REACH)' to reduce animal testing in the EU, a call on a global ban for animal testing in cosmetics by the EU, and increasing adoption of non-animal alternative testing technologies by major industries are also some of the factors.

Drivers Of The Animal Testing Market

The need for preclinical studies for the approval of therapeutics, increasing investment in R&D by the pharmaceutical companies, advances in genetic engineering, and the complexity of biologics are the factors that drive the animal testing market.

The Need For Preclinical Studies For The Approval Of Therapeutics

The need for preclinical studies is on the rise as the researchers gain insights on new drug candidates' dosing and toxicity while conducting these studies in animal models. Preclinical studies provide information about the safety and efficacy of a drug candidate before testing it in humans. The studies require appropriate preclinical models that are comparable to the target population to ensure reliable results. According to clinicalTrials.gov, a web-based resource which provides data on clinical studies, as of February 2020, there were 330,113 clinical studies registered, of which 34% were from the USA.[xlii]

With the growing need for drug discovery and development, the need for animal models in preclinical studies is also growing.[xliii]

Increasing Investment In R&D By The Pharmaceutical Companies

The rate of investment has been increasing over the years and pharmaceutical companies are the top investors in R&D. The key factor for research-based pharmaceutical companies investing more in R&D is the discovery and development of new drugs serving unmet medical needs. For FY20-21, the average R&D expenses of pharma companies in India were 7.2% of total revenues, with Lupin, Alembic Pharma, and Dr. Reddy's spending more than others. In the FY20-19, the top ten pharmaceutical companies spent approximately Rs 10,627 crore ($1.43 billion) on R&D. After taking into account the cumulative expenditure of other small and medium-sized players in the Indian pharmaceutical industry, this figure was around Rs 22,500 crore ($3.03 billion). [xliv]

With the increasing investment in novel therapeutics development, animal models will be widely employed in pharmaceutical research. This factor is therefore expected to drive the animal testing market.

Advances In Genetic Engineering

Studies involving genetically engineered animal models provide important clues about the underlying mechanisms that can make researchers understand the pathology of a disease. The growing interest in modeling human diseases using genetically modified animal models has led to the development of several gene targeting and gene editing methods.

Recent advances in genome editing technologies reflect the rapid development of engineered endonucleases including zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and clustered regularly interspaced short palindromic repeat (CRISPR) systems. Using these systems, researchers are now able to rapidly generate disease-associated animal models for a wide range of species.[xlv] Therefore, the advances in genetic engineering technologies are driving the animal testing market.

The Need For Animal Models To Understand The Complexity Of Biologics

The molecular structure, size, manufacturing, storage, and administration as well as the potential to cause adverse effects, all these contribute to the complexity of biologics. It is important to ensure the safety and efficacy of these complex biologics for human use. Animal models are used for a proper understanding of biologic drug candidates' complexity, and predict human response to these drugs.[xlvi, xlvii]

Therefore, the increasing need for biologic drugs is driving the requirement for animal models, thereby contributing to the growth of the animal testing market.

Restraints On The Animal Testing Market

The high cost of animal studies, the requirement of a large number of animals for research studies, ethical concerns on animal experimentations, stringent regulations, and the threat from alternatives are the factors restraining the animal testing market.

The High Cost Of Animal Studies

The high cost associated with animal testing is challenging the growth of this market. The total cost of animal use in research studies is the sum of the cost of acquisition of the animals and that of maintaining the animals prior to and during their use. The maintenance cost and the actual cost for a particular species vary with the sex, strain, weight, age, quantity ordered, method of shipping, and distance shipped.[xlviii] According to an animal supply company, New Zealand White Rabbits cost as high as $352 each, purebred Beagles for $1,049 and some primates costing more than $8,000 each.[xlix] Additionally, there is human labor cost, as the animals need an attendant.

The high cost of animal studies is hindering the animal testing market, and in a way boosting the adoption of alternative testing methods.

The Requirement Of A Large Number Of Animals For Research Studies

The requirement for a large number of animals is likely to challenge the growth of the animal testing market. According to 'The Nuffield Council on Bioethics' report, the number of animals that are experimented on globally ranges from 50 to 100 million. It is difficult to obtain an accurate figure but different sources estimate that around 100 million vertebrates are used for research purposes. According to the UK government, around 2.88 million animals were used in Great Britain for scientific, medical and veterinary research.[l] Approximately half of all procedures were for experimental purpose (1.44 million). The remaining half was allocated to the development and breeding of genetically altered (GA) animals (1.44 million). In 92% of all procedures, mice, fish, or rats were used. For the past decade, these have been the most commonly used species. [li]

Every year millions of experiments are being conducted and millions of experimental animals are being used. In 2019, 797,546 laboratory animals were used for research in US.[lii] A large number of animals require a skilled workforce for housing and handling of these animals and are quite expensive. Therefore, the growing need for a large number of animals may hinder the growth of the market.

Ethical Concerns On Animal Experimentations

Experimentation on animals is morally unacceptable especially if the experiments are causing pain and suffering to them. Although animal experiments have immensely contributed towards the understanding of various disease processes and in developing better treatment methods, a lot of opposition does exist for the use of animals for research purposes. Worldwide, many organizations protest against animal experimentations. This factor is greatly hampering the animal testing market.

Stringent Regulations

Many regulatory bodies that pose restrictions over the use of animal models have formed in various countries for humane use and care of animals used for experiments. Some of the regulatory bodies include the International Council for Laboratory Animal Science, Council for International Organizations of Medical Sciences, International Union of Biological Sciences, and International Committee on Laboratory Animals. [liii] The research should be conducted in compliance with regulatory provisions, which cover the inspection of animal premises, licensing of the premises, and regulatory training of the research personnel involved in the project - who perform animal procedures and take care of animals, and the mandatory authorization of every project by an Animal Ethics Committee, after ethical evaluation. The animal research study that is not compliant with any of the regulatory bodies is not licensed.[liv]

Globally, a variety of laws has been passed for animal care and protection. Animals should be used in research only if,

- The designed experiment will significantly advance the present knowledge and understanding of the subject
- Lead to improvement in care
- Leads to new treatments and cures
- The research projects are designed in a way that requires a minimal number of animals
- The use of animals in biomedical research that does not cause pain to the animal
- There are no suitable alternatives

The stringent regulatory framework for the protection of animals, is, hindering the growth of the animal testing market.

USA Animal Testing And Non-Animal Alternative Testing Market

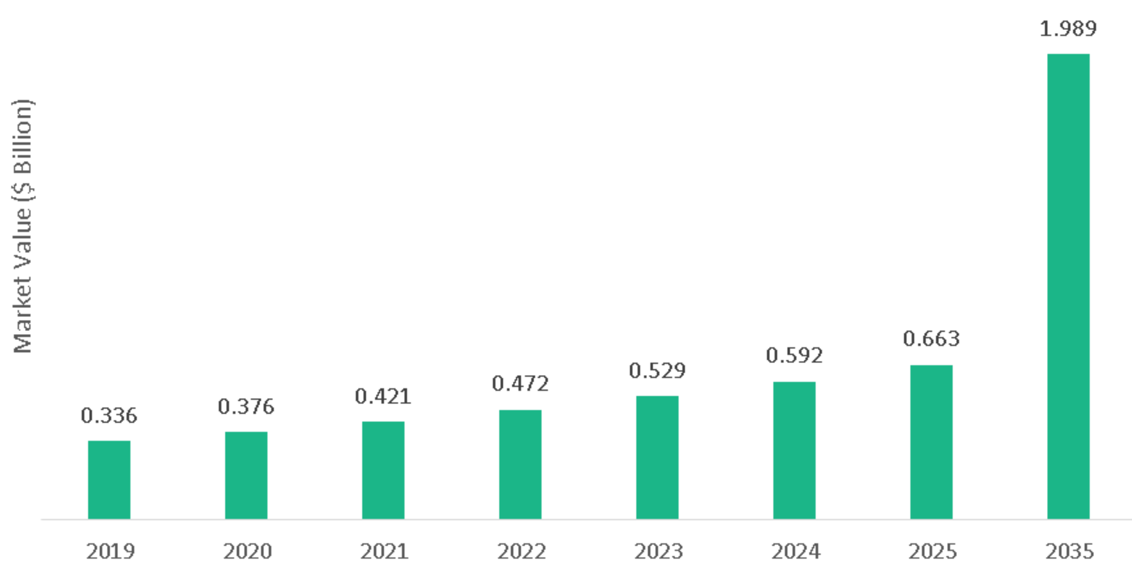
USA Non-Animal Alternative Testing Market

USA non-animal alternative testing market is supported by the adoption of the 3R principle by regulatory agencies, increasing the adoption of alternative technologies and end-user companies. 3Rs alternatives refers to reduction, refinement and replacement of animals used in research, testing and education. The 3Rs principle is implicit in the Animal Welfare Act US that makes it important for any scientists planning to do an experiment to demonstrate why there is no alternative.[lv] High adoption of technologies such as organs-on-chips (OOCs) and 3D cell culture in the pharmaceuticals and medical devices industries as an alternative to animal testing will also drive the non-animal alternative testing market. For instance, in March 2021, Emulate Inc, a US-based biotechnology company launched a colon intestine chip that will accelerate the identification of drug candidates to treat inflammatory damage in the colon. This chip is launched to target pharma and biotech companies, academics, and other researchers.[lvi]

USA Non-Animal Alternative Testing Market Value ($ Billion)

The chart and table below show the year-on-year growth of the USA non-animal alternative testing market during 2019 – 2035.

Figure 5: USA Non-Animal Alternative Testing Market Size, 2019 – 2035, $ Billion



The Business Research Company
Sources: *National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary*

Table 5: USA Non-Animal Alternative Testing Market Size, 2019– 2035, $ Billion

Market	2019	2020	2021	2022	2023	2024	2025	2035	CAGR (2019-2025)	CAGR (2025-2035)
Non-Animal Alternative Testing	0.336	0.376	0.421	0.472	0.529	0.592	0.663	1.989	11.99%	11.61%

The Business Research Company
Sources: *National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary*

The USA non-animal alternative testing market grew from $0.336 billion in 2019 to $0.663 billion in 2025 at a compound annual growth rate (CAGR) of 11.99% and to $1.989 billion in 2035 at a compound annual growth rate (CAGR) of 11.61%.

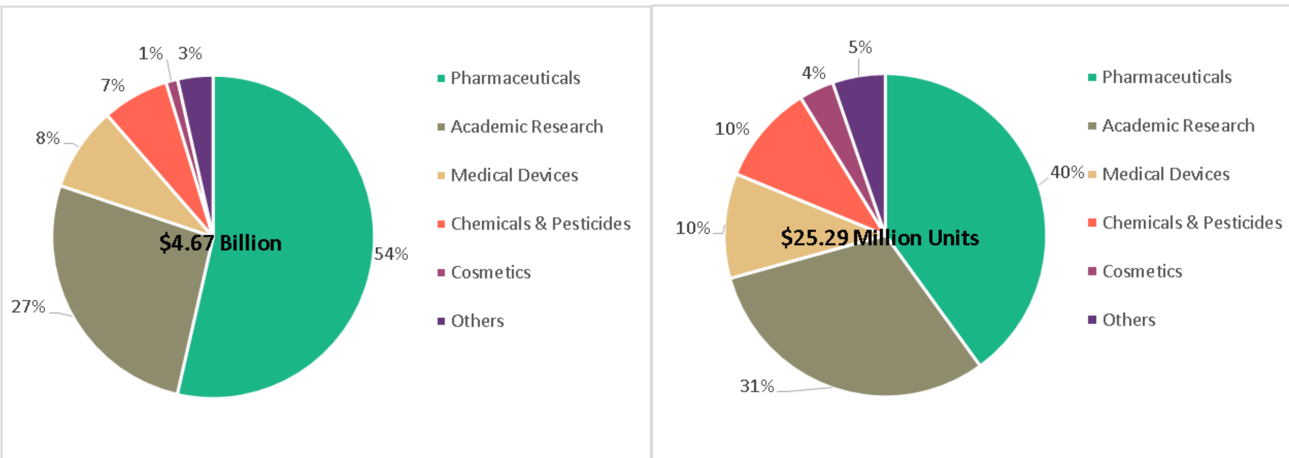
USA Animal Testing Market By End Use Industrial Application

This section covers the segmentation of the USA animal testing market by end-use industrial application.

Market By Value And Volume

The chart below shows the USA animal testing market by end-use industrial applications by value and by volume (number of animals used):

Figure 6: USA Animal Testing Market, By End Use Industrial Application, By Value ($ Billion), And By Volume (Millions) 2019



The Business Research Company
Sources: National Statistics Offices, UN Comtrade, TBRC Analysis, TBRC Estimates, TBRC Secondary

Table 6: USA Animal Testing Market, By End Use Industrial Application, By Value ($ Billion), And By Volume (Millions) 2019,

Segmentation	Share Of The Market by Value (2019)	Market Value (2019, $ billion)	Share Of The Market by Volume (2019)	Market Volume (2019, $ billion)
Pharmaceuticals	53.6%	2.50	40.00%	10.12
Academic Research	26.6%	1.24	30.70%	7.77
Medical Devices	8.4%	0.39	10.50%	2.66
Chemicals & Pesticides	6.7%	0.31	10.00%	2.53
Cosmetics	1.2%	0.05	3.50%	0.89
Others	3.5%	0.17	5.30%	1.34

The Business Research Company
Source: TBRC Primary[lvii], TBRC Analysis

Pharmaceuticals industry was the largest end-user market of the USA animal testing market and accounted for $2.50 billion or 53.6% of the animal testing market by value, and 10.12 million units or 40% of the market by volume in 2019.

Academic Research industry was the second largest end-user market of the USA animal testing market and accounted for $1.24 billion or 26.6% of the animal testing market by value, and 7.77 million units or 30.70% of the market by volume in 2019.

Medical Devices industry was the third largest end-user market of the USA animal testing market and accounted for $0.39 billion or 8.4% of the animal testing market by value, and 2.66 million units or 10.50% of the market by volume in 2019.

Chemicals And Pesticides industry was the fourth largest end-user market of the USA animal testing market and accounted for $0.31 billion or 6.7% of the animal testing market by value, and 2.53 million units or 10.00% of the market by volume in 2019.

Cosmetics industry was the smallest end-user market of the USA animal testing market and accounted for $0.05 billion or 1.2% of the animal testing market by value, 0.89 million units or 3.50% of the market by volume in 2019.

Other industries were the fifth largest end-user market of the USA animal testing market and accounted for $0.17 billion or 3.5% of the animal testing market by value, and 1.34 million units or 5.30% of the market by volume in 2019.

The high share of the market for pharmaceuticals and academic research segments can be attributed to a greater number of animals being used in these industries, coupled with the use of high cost genetically altered animals. The others segment includes animal testing on tobacco, biocides, and animal feed. Most industries including pharmaceuticals, chemicals & pesticides, and medical devices outsource their animal testing to contract research organizations (CROs).

In the USA, more than 80% of all laboratory animals are used by the pharmaceutical, academic research, and medical device industries. The largest share for the pharmaceuticals can be attributed to the FDA's requirement for animal testing to validate safety and efficacy for each new molecule before approving for clinical trials.

The second-largest share for academic research can be attributed to government funding, and corporate funding to conduct research studies for drug development. For instance, NIH provides 47% of its funds for animal research every year. The share for medical devices can be attributed to the FDA's mandate for medical devices to undergo preclinical testing on animals before submitting to FDA for authorization. The chemical & pesticide segment has a 10% share of the market, which can be attributed to regulatory (EPA's) mandate to test new chemicals and pesticides on animals for toxicology profile.

The cosmetic industry's share can be attributed to lack of mandatory regulations from federal agencies for animal testing, protests from animal welfare organizations to reduce and stop animal testing, and customer preference towards cosmetics with cruelty-free products.

Share Of Top 5 Companies, By Revenue (In Each Industrial Application)

The table below shows the share of the top five companies in each industrial application, by share of the total number of animals used in the USA:

Table 7: USA Animal Testing Market, Estimated Share of Top 5 Companies (In Each Industrial Application), 2020

Industry	Top 5 Companies	Company Share	CRO's Share	Others
Pharmaceuticals				
	Novartis	3.7%	50.0%	35.7%
	Merck & Co	3.6%		
	Pfizer	3.1%		
	AbbVie	2.9%		
	Sanofi	1.0%		
	Total Share (top 5 companies)	**14.3%**		
Medical Devices				
	Medtronic	8.2%	70.0%	13.4%
	GE Healthcare	3.8%		
	Abbott Laboratories	2.0%		
	Danaher Corporation	1.5%		
	Johnson & Johnson	1.1%		
	Total Share (top 5 companies)	**16.6%**		
Chemicals & Pesticides				
	DuPont de Nemours	3.2%	80.0%	12.0%
	Dow chemical	2.3%		
	LyondellBasell Industries	1.4%		
	PPG Industries, Inc.	0.6%		
	Ecolab Inc.	0.5%		
	Total Share (top 5 companies)	**8.0%**		

The Business Research Company
Source: Annual Reports[lviii,lix,lx,lxi,lxii,lxiii,lxiv,lxv,lxvi,lxvii,lxviii,lxix,lxx,lxxi,lxxii] CRO[lxxiii], TBRC Analysis

In the USA, animal testing is prominent in three major industries: pharmaceuticals, medical devices, and chemical & pesticides. The pharmaceutical industry is the major one with in-house animal testing, and outsourcing to clinical research organizations (CROs). In pharmaceuticals, outsourcing to CROs has a 50% share of USA pharmaceutical animal testing market.[lxxiv] The top five pharmaceutical companies such as Novartis, Merck, Pfizer, Abbvie and Sanofi have a 14.3% share of the total USA animal testing market in the pharmaceutical segment. This is mainly due to the in-house allocation of funds for animal testing in drug discovery and development. The other pharmaceutical companies have a 35.7% share of the total USA pharmaceutical animal testing market.

The medical device industry and chemical industry depend mainly on CROs for animal testing. In the medical device and chemical industries, outsourcing to CROs have a 70% and an 80% share of the total USA medical device animal testing market respectively. The top five medical device companies such as Medtronic, GE Healthcare, Abbott Laboratories, Danaher Corporation, and Johnson & Johnson have a 16.6% share of the total USA animal testing market in the medical device segment. Other medical device manufacturers have a 13.4% share of the total USA medical device animal testing market.

The top five chemical and pesticide companies such as DuPont, Dow chemicals, LyondellBasell, PPG Industries and Ecolab have an 8% share of the USA cosmetics & pesticides animal testing market. The other chemical and pesticide manufacturers have a 12% share of the USA cosmetics & pesticides animal testing market in the chemicals and pesticides segment.

Europe Animal Testing And Non-Animal Alternative Testing Market

Regulatory Landscape In Europe

The Directive on the protection of animals used for scientific purposes (2010/63), the Regulation on cosmetic products (1223/2009), REACH (2007/2006) and Classification, Labelling and Packaging (CLP) (1272/2008) are examples of EU legislation that require, or strongly encourage, the replacement of animal testing.[lxxv]

The animal testing for cosmetic products is forbidden in the EU with a 2004 amendment to Cosmetics Directive 'The Council Directive 76, '/768/EEC of 1976-07-27 on the approximation of the laws of the Member States relating to cosmetic products'. Animal testing for cosmetic ingredients is also prohibited since March 2009. Cosmetics Directive amendment, since 11 March 2009, has prohibited to market cosmetic products containing ingredients which have been tested on animals.

With regards to animal testing for cosmetic products, Chapter V, Article 18 of Regulations EC No 1223/2009 of the European Parliament and of the Council of 2009 on cosmetic products prohibits to test finished cosmetic products and cosmetic ingredients on animals (testing ban). The same article also prohibits the marketing of finished cosmetic products and ingredients in the EU that were tested on animals (marketing ban). [lxxvi]

EU Directive 2010/63

Experiments on vertebrate animals in the European Union are subject to Directive 2010/63/EU since January 1, 2013. The regulation protects animals used for scientific purposes was finalized in November 2010. This is an updated Directive that has replaced the Directive 86/609/EEC on the protection of Animals used for Experimental and other scientific purposes, adopted in 1986.

EU Directive 2010/63 is the regulation guiding the protection of animals used for scientific purposes in EU member states. The Directive was adopted in 2010, but member states were given until January 2013 to transpose these regulations into domestic law. The purpose of the Directive is to harmonize standards across the EU, as well as to promote and implement the 3Rs – Replacement, Refinement and Reduction of animals used for research.

The Directive laid down minimum standards for housing and care, and systematic project evaluation.

According to the2010/63/EU – Preamble. Section 11,

- The care and use of live animals for scientific purposes is governed by internationally established principles of replacement, reduction and refinement.
- To ensure that the way in which animals are bred, cared for and used in procedures within the Union is in line with that of the other international and national standards applicable outside the Union, the principles of replacement, reduction and refinement should be considered systematically when implementing this Directive.
- When choosing methods, the principles of replacement, reduction and refinement implemented through a strict hierarchy of the requirement to use alternative methods.
- Where no alternative method is recognized by the legislation of the Union, the numbers of animals used may be reduced by resorting to other methods and by implementing testing strategies, such as the use of in vitro and other methods that would reduce and refine the use of animals.

The Directive demands that methods selected should use the minimum number of animals that would provide reliable results and require the use of species with the lowest capacity to experience pain, suffering, distress or lasting harm that are optimal for extrapolation into target species (Directive 2010/63/EU – Preamble. Section 13).

The legislation covers non-human vertebrate species (including independently feeding larval forms and last trimester fetal forms of mammals) and cephalopods. [lxxvii,lxxviii]

Appendix

Glossary

Animal Testing: Animal testing is also known as animal experimentation, animal research and in-vivo testing. Animal testing is a procedure performed on living animals for scientific research into basic biology and diseases, assessing the effectiveness of new medicinal products for human use.[lxxix] Animal testing helps to understand potential intended effects and side effects of chemicals and products on humans.[lxxx,lxxxi]

Assay: It is an analysis performed to qualitatively assess or quantitatively measure the presence, amount or functional activity of a target entity.[lxxxii]

Academic research: Academic research is the systematic investigation into a problem or situation, where the intention is to identify facts and/or opinions that will assist in solving the problem or dealing with the situation.[lxxxiii]

Non-Animal Alternative Technologies: Non-animal technologies are alternatives to using animals for efficacy and safety in testing pharmaceuticals, veterinary medicines, agrochemicals, chemicals, and consumer products. Alternatives to animal testing include sophisticated tests using human cells and tissues (in-vitro methods), advanced computer-modeling techniques (in-silico models), and studies with human volunteers. [lxxxiv,lxxxv]

Animal House: Animal house is a shelter for big and small animals such as mice, rats, mice.[lxxxvi]

Animal Cage: A box or enclosure having openwork for confining or carrying animals (such as birds).[lxxxvii]

Animal Food: Animal feed is food given to domestic animals in the course of animal husbandry.[lxxxviii]

Animal Bedding: Animal bedding is a space used to support their bodies for resting or when otherwise stationary.

Animal Welfare: Animal welfare is the conditions in which it lives. An animal is in a good state of welfare if it is healthy, comfortable, and well nourished, safe and able to express innate behavior.[lxxxix]

Animal Efficacy Rule: The rule permits the FDA Agency to approve drugs or license biological products based on animal efficacy studies for use in ameliorating or preventing serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances.[xc]

ADME (absorption, distribution, metabolism, and excretion): ADME is a pharmacokinetic action of a chemical drug such as absorption, distribution, metabolism, and excretion in the human body.[xci]

Biopharmaceuticals: Biopharmaceuticals are medical drugs produced by using biotechnology. They include proteins (including antibodies), and nucleic acids (DNA, RNA or antisense oligonucleotides).[xcii]

Basic Research: Scientific research that aims to improve scientific theories for improved understanding or prediction of natural or other phenomena.[xciii]

Biocide: It is a chemical substance or microorganism intended to destroy, deter, render harmless or exert a controlling effect on any harmful organism by chemical or biological means.[xciv]

Biomarker: A substance measured in a biological system as an indicator of exposure, effect, susceptibility, or clinical disease.[xcv]

Biochemistry: Biochemistry is the science in which chemistry is applied to the study of living organisms and the atoms and molecules, which comprise living organisms.[xcvi]

Bovine Corneal Opacity And Permeability (BCOP) Test: The Bovine Corneal Opacity and Permeability test method (BCOP) is an in-vitro test method that can be used to classify substances as ocular corrosives and severe irritants.[xcvii]

Cosmetics: Cosmetics are substances or products used to enhance or alter the appearance of the face or fragrance and texture of the body. Many cosmetics are designed for use of applying to the face and body.[xcviii]

Computer Simulations: A computer simulation or a computer model is a computer program and a mathematical tool to simulate an abstract model and gain insights into the operation of a particular system.[xcix]

Clinical Research Organizations (CRO): A CRO is an organization contracted by the pharmaceutical, biotechnology, medical device industries to manage and lead clinical trials and other research support services.[c]

Clinical Trial: A clinical trial is a research program conducted with patients to evaluate a new medical treatment, drug, or device.[ci]

Cynomolgus Macaques: Cynomolgus macaques also known as the long-tailed or crab-eating macaque are non-human primates (NHP) commonly used in biomedical research.[cii]

Chromosome Aberration Toxicity Test: It is an in-vitro chromosomal aberration test to identify agents that cause structural chromosomal aberrations in cultured mammalian cells.[ciii]

Corrositex Membrane Barrier: Corrositex is an in-vitro method used to determine the dermal corrosive potential of chemicals and chemical mixtures. It is a replacement for the dermal corrosivity rabbit test.[civ]

Drug Efficacy: It refers to the ability of a drug or treatment to provide a therapeutic effect.[cv]

Disease Modeling: It is a tool to help researchers understand the pathogenesis or mechanisms behind a specific disease.[cvi]

Draize Rabbit Eye Test: It is an in-vivo acute ocular toxicity test to provide a method for assessing the irritation potential of materials that are exposed to human eyes, such as environmental chemicals.[cvii]

Draize Rabbit Skin Test: It is an in-vivo acute ocular toxicity test to provide a method for assessing the irritation potential of materials that are exposed to human skin, such as environmental chemicals.[cviii]

Environmental Protection Agency (EPA): An agency enforces environmental regulations to protect people and the environment from significant health risks.[cix]

Endocrine Disruptor Screening Program: It is an approach to screen pesticides, chemicals, and environmental contaminants for their potential effect on estrogen, androgen, and thyroid hormone systems.[cx]

EpiDerm Human Skin Model: It is a skin model that constitutes of reconstructed human epidermis obtained from human-derived non-transformed epidermal keratinocytes, which closely mimic the histological, morphological, biochemical, and physiological properties of the epidermal layer of human skin.[cxi]

Genetic Toxicity: Genotoxicity tests are used to assess the potential of the chemical substance to induce gene mutations or chromosome damage in bacterial, mammalian cells in-vitro, and in-vivo test systems.[cxii]

Guinea pig maximization test: Guinea pig maximization test is an in vivo test to screen for substances that cause human skin sensitization.[cxiii]

Human Corneal Epithelium Eye Irritation Test (HCE EIT): It is an in-vitro non-animal test method for identifying chemicals and mixtures that cause irritation to the corneal epithelium.[cxiv]

High Throughput Model: High-throughput screening (HTS) model is a method for scientific experimentation especially used in drug discovery and relevant to the fields of biology and chemistry.[cxv]

Human Physiology: Human physiology is the science of the mechanical, physical, and biochemical functions of normal humans or human tissues or organs.[cxvi]

Hybrid: Hybrid is an offspring of two animals or plants of a different race, breeds, varieties, species, or genera.[cxvii]

Human Blood Method (Endosafe-IPT): It is an in-vitro test to detect pyrogens from blood in combination with a solution believed to contain pyrogens

In Vitro Cell: In-vitro cell refers to a living cell in a test tube or laboratory dish.[cxviii]

In Vivo Toxicology: It is the study of toxic effects of chemical substances in animals based on statistical and quantitative analysis.[cxix]

In-vitro Technologies: These are technologies or procedures performed outside the living organism using cells and tissues in an artificial biological system.[cxx]

In-silico Technologies: These are computer program-based technologies using computational mathematical tools to characterize biological experiments on a computer.[cxxi]

In Vitro Reconstructed Human Epidermis (RhE) Test: A skin corrosion test allows the identification of corrosive chemical substances on a three-dimensional human skin model. It comprises of at least a reconstructed epidermis with a functional stratum corneum.[cxxii]

Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM): It is a permanent committee of the National Institute of Environmental Health Sciences (NIEHS) under the NTP's Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM). It promotes the regulatory acceptance of test methods that protect human and animal health and the environment while reducing, refining, or replacing the use of animal tests.[cxxiii]

Inbred: Inbred is the production of offspring from the mating or breeding of individuals or organisms that are closely related genetically.[cxxiv]

Immunodeficient Model: These are models with immunodeficient characteristics used for immunology, infectious disease, cancer, stem cell biology, and other research.[cxxv]

Induced Pluripotent Stem Cells (iPSCs): These are adult cells, which have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells.[cxxvi]

Local Lymph Node Assay (LLNA): It is a murine model developed to evaluate the skin sensitization potential of chemicals. The assay relies on the measurement of events induced during the induction phase of skin sensitization, specifically lymphocyte proliferation in the draining lymph nodes that is a hallmark of a skin sensitization response.[cxxvii]

Limulus Amoebocyte Lysate (LAL): It is an aqueous extract of blood cells from the Atlantic horseshoe crab (which is species of arthropod).[cxxviii]

Medical Devices: Medical devices are products or equipment intended generally for a medical use.[cxxix]

Non-human primates: Non-human primates refer to animals such as monkeys, apes, and chimpanzees.[cxxx]

National Institutes of Health (NIH): It is a part of the US Department of Health and Human Services. It is involved in making important discoveries that improve health and save lives.[cxxxi]

NTP Interagency Center For The Evaluation Of Alternative Toxicological Methods (NICEATM): It is a National Toxicology Program (NTP) office focused on the development and evaluation of alternatives to animal use for chemical safety testing.[cxxxii]

National Institute Of Environmental Health Sciences (NIEHS): This institute fund centers for environmental health studies at universities across the United States.[cxxxiii]

National Toxicology Program (NTP): The National Toxicology Program provides the scientific basis for programs, activities, and policies that promote health or lead to the prevention of disease. It helps in generating, interpreting, and sharing toxicological information about potentially hazardous substances in the environment.[cxxxiv]

Organ-on-chip (OOC): It is a multi-channel 3-D microfluidic cell culture chip that simulates the activities, mechanics and physiological response of entire organs and organ systems.[cxxxv]

Organization for Economic Co-operation and Development (OECD): It is an international organization which works together with governments, policymakers and citizens; The organization works on establishing international norms and finding evidence-based solutions to a range of social, economic and environmental challenges

Organotypic In Vitro Systems: It is an in-vitro culture system that organotypic culture system (OCS) allows for the in vitro growth of complex biological tissues in a way that replicates part of their normal physiology and function.[cxxxvi]

Outbred: Outbred is the production of offspring from the mating or breeding of individuals or organisms that are from different breeds and no common ancestors.[cxxxvii]

Preclinical: Preclinical is research using animals to find out if a drug, procedure, or treatment is likely to be useful.[cxxxviii]

Pharmacokinetics: Pharmacokinetics (PK) is the study of drug absorption, distribution, metabolism, and excretion after its delivery to an organism.[cxxxix]

Pesticides: A pesticide is a substance used to kill, repel, or control certain forms of plant or animal life that are pests.[cxl]

Pharmaceutical: Pharmaceutical is a drug derived from organic or inorganic chemicals and used to treat a wide range of medical conditions.[cxli]

People For The Ethical Treatment of Animals (PETA): PETA is a non-governmental organization (NGO) committed to ending the abusive treatment of animals in business and society.[cxlii]

Pharmaceuticals And Medical Devices Agency (PMDA): PMDA is the government organization in Japan in charge of reviewing drugs and medical devices, overseeing post-market safety, and providing relief for adverse health effects.[cxliii]

Pharmacodynamics: It is the quantitative study of the relationship between drug exposure (concentrations or dose) and pharmacologic or toxicological responses.[cxliv]

Personalized Medicine: Personalized medicine (PM) is an extension of traditional medicine that has the potential to tailor therapy with the best response and highest safety margin to ensure better patient care.[cxlv]

Pharmacology: The science that deals with the origin, nature, chemistry, effects, and uses of drugs includes pharmacokinetics, pharmacodynamics, and toxicology.[cxlvi]

Quantitative Structure-Activity Relationships (QSARs): It is a method to derive certain effects or properties of chemical substances in the absence of experimental data.[cxlvii]

Organoids: Organoids are tiny, self-organized three-dimensional tissue cultures derived from stem cells.[cxlviii]

Regulatory Approval: It is a license, registration or authorizations that are necessary for the manufacture, distribution, use, sale, and marketing of a Licensed Product for human therapeutic or prophylactic use in a regulatory jurisdiction.

Reproductive Toxicity Testing: Reproductive toxicity tests assess a substance's tendency to cause reproductive system effects.[cxlix]

Reconstructed Human Cornea-Like Epithelium In Vitro Are-Nrf2 Luciferase Test: It is an in-vitro procedure allowing the identification of chemicals that cause eye irritation or serious eye damage by using reconstructed human cornea-like epithelium (RhCE) which closely mimics the histological, morphological, biochemical and physiological properties of the human corneal epithelium.[cl]

Rhesus Macaques: These are non-human primates used in biomedical research.[cli]

Rat Phototoxicity Test: This test is used to identify the phototoxic effect of a test substance induced by the combination of test substance and light.[clii]

Rat Developmental Toxicity Test: This test is used to identify adverse effects induced during pregnancy, or because of parental exposure manifested at any point in the life span of the organism.[cliii]

Rat Limb Bud Test: An in-vitro test evaluates the effects of a test substance on the differentiation and growth of micro mass cultures of the rat limb bud.[cliv]

Rabbit Pyrogen Test: The pyrogen test on rabbits is used to measure the increase in the rabbit's temperature upon injection with a pyrogen (substance) that could contain a contaminant of the pyrogen type.[clv]

Rat Hershberger Assay: The Hershberger Bioassay is an in-vivo short–term screening test to evaluate the ability of a chemical to elicit biological activities consistent with androgen agonists, antagonists or 5 á-reductase inhibitors.[clvi]

Rat Uterotrophic Assay (OVX): The Uterotrophic Bioassay is a short-term screening test to evaluate the ability of a chemical to elicit biological activities consistent with agonists or antagonists of natural estrogens (e.g. 17ß-estradiol).[clvii]

Receptor Binding Assay: This is the important component in lead identification and lead characterization process used to characterize the most known drug targets.[clviii]

Synthetic Skin Substitutes: Synthetic skin substitutes are non-biological molecules and polymers that are stable, biodegradable and provide an adequate environment for the regeneration of tissue.[clix]

Skin Irritation: Skin irritation refers to the production of reversible damage to the skin occurring after exposure to a substance or mixture.[clx]

Skin Corrosion: Skin corrosion refers to the production of irreversible damage to the skin after exposure to a substance or mixture.[clxi]

Stakeholder: A person, group or organization that has interest or concern in an organization.[clxii]

Skin Sensitization: Skin sensitization is an allergic response to a substance after skin contact.[clxiii]

Systemic Toxicity: These are toxic effects due to the absorption and distribution of a toxicant or chemical to a site distant from its entry point.[clxiv]

Stem Cell Biology: Stem cells are as precursor cells that have the capacity to self-renew and to generate multiple mature cell types.[clxv]

Squirrel Monkeys: These are the small species of New World monkey that is natively found in the forests and tropical jungles of Central and South America.[clxvi]

Sister Chromatid Exchange Toxicity Testing: The in vivo sister chromatid exchange (SCE) toxicity test detects the ability of a chemical to enhance the exchange of DNA between two sister chromatids of a duplicating chromosome.[clxvii]

Syrian Hamster Embryo (SHE) Cell Transformation Test: The Syrian hamster embryo (SHE) cell transformation assay (CTA) is short-term in vitro assay recommended as an alternative method for testing the carcinogenic potential of chemicals.[clxviii]

Toxicity Testing: The test is designed to generate data concerning the adverse effects of a substance on human or animal health, or the environment.[clxix]

Tissue Cultures: It is a method of biological research in which fragments of tissue from an animal or plant are transferred to an artificial environment in which they can continue to survive and function.[clxx]

Toxicology Profiling: Toxicology profiling is a unique compilation of toxicological information on a given hazardous substance.[clxxi]

Therapeutic Antibodies: Therapeutic antibodies are synthetic substances that are able to bind to specific proteins on the surfaces of cells.[clxxii]

Toxic Substances Control Act (TSCA): The Toxic Substances Control Act (TSCA) is a law, administered by the US Environmental Protection Agency (EPA) that regulates the introduction of new or already existing chemicals.[clxxiii]

Transgenic Mouse Models: The transgenic mouse model refers to animal models in which DNA from the mouse genome or from the genome of another species has been incorporated into each cell of the mouse model genome.[clxxiv]

Translational Rats: Rats manipulated for translational research purposes.

U-SENS: It is an in-vitro skin sensitization method based on the human myeloid U937 cell line to assess the skin sensitization potential of substances.[clxxv]

Unscheduled DNA Synthesis Toxicity Test: Unscheduled DNA synthesis (UDS) test with mammalian cells in-vivo is to identify substances that induce DNA repair after excision and removal of a stretch of DNA containing a region of damage induced by chemical substances (solid or liquid) or physical agents in the cell.[clxxvi]

3T3 Neutral Red Uptake Test: It is an in-vitro test used to identify the phototoxic potential of a test substance induced by the excited chemical after exposure to light.[clxxvii]

Market Data Sources

Table 8: Market Data Sources

Company	Link
MatTek	https://www.mattek.com/reference-library/program-to-reduce-animal-testing-for-epa-registrations-of-antimicrobial-products/
BioIVT	https://www.bioivt.com/application_area/adme-toxicology/
L'Oréal	https://www.cnbc.com/2017/05/25/loreal-is-making-lab-produced-human-skin-to-curb-animal-testing.html
KIYATEC	http://kiyatec.com/
RegeneMed, Inc.	http://www.regenemed.com/
In Vitro ADMET Laboratories (IVAL)	https://invitroadmet.com/about/letter-from-ceo/
Creative Scientist, Inc.,	https://www.cscientist.com/cell-based-toxicology
Promega	https://www.promega.in/responsibility/product-reach-article/providing-alternatives-to-animal-testing/
Cyprotex	https://www.cyprotex.com/
AllCells, LLC	https://www.allcells.com/tissue-products/bone-marrow/
Cellular Dynamics	https://fujifilmcdi.com/why-cdi/drug-discovery/
StemoniX	https://stemonix.com/
Stemina	https://stemina.com/products-and-services/devtox-quickpredict/
JRF Global	https://www.jrfglobal.com/about/about-jrf-global.aspx
PharmaCo-Cell Company Ltd.	https://www.pharmacocell.co.jp/en/
China Tissue Engineering Co.Ltd (Fujifilm Group)	http://www.jpte.co.jp/english/
ReproCELL, Inc.	https://www.reprocell.com/
Vessel Inc.	https://www.jstage.jst.go.jp/article/aatex/23/2/23_aatex23_53/_pdf/-char/en
O'Atari Inc.	https://oatari-inc.com/about-us/
AxoSim	https://axosim.com/nerve-on-a-chip/

Emulate Bio	https://www.emulatebio.com/our-technology
TissUse	https://www.nortisbio.com/#applications
InSphero	https://insphero.com/media-release/insphero-organ-on-a-chip-solutions-featured-in-slas-technology/
Tara Biosystems	https://tarabiosystems.com/platform/
CN Bio Innovations, Ltd	http://www.jthaten.de/2018%20VDI%20IAP%20TissUse.pdf
Hesperos	https://hesperosinc.com/technology/
AlveoliX	http://www.alveolix.com/technology/
CN Bio	https://cn-bio.com/organ-on-chip/
SynVivo, LLC	https://www.synvivobio.com/microfluidic-chips-3/
Mimetas	https://mimetas.com/page/technology
Mimetas	https://mimetas.com/page/technology
Micronit	https://www.micronit.com/products/organ-on-a-chip.html
Kyoto University	https://www.kyoto-u.ac.jp/en/research/research_results/2017/170725_2.html
Osaka University	https://selectbiosciences.com/conferences/index.aspx?conf=3D2016
Cyprotex	https://www.cyprotex.com/insilico/physiological_modelling/chempk
Leadscope	http://www.leadscope.com/toxicity_databases/
MultiCASE Inc	http://www.multicase.com/
ScitoVation (QSAR models)	https://www.scitovation.com/what-we-do/predictive-tools/
IOMICS Corporation (FUSION Analytics Platform™)	https://iomics.us/
Simulations Plus Inc.	https://www.simulations-plus.com/
In Silico Biosciences, Inc	http://www.in-silico-biosciences.com/
Applied BioMath	https://www.appliedbiomath.com/applying-scientific-expertise/capabilities

Nuventra	https://www.nuventra.com/
Interprotein Corporation	http://www.interprotein.com/intendd.html
Modulus Discovery, Inc.	https://modulusdiscovery.com/
Organ Technologies, Inc.	https://www.Chinatimes.co.jp/tag/organ-technologies-inc/
EPISKIN	https://www.episkin.com/About%20us

Research Methodology

The Business Research Company's reports are based on the methodology below.

Global Market Model (GMM)

The Global Market Model is a comprehensive database of integrated market information which covers historic, current and forecast market information. This database helps in drawing multiple conclusions, exploring market opportunities and taking effective business decisions.

Global Market Model's methodology ensures that the data is of the highest quality. It starts with high standard data sources and correlation-based modelling techniques. This is supported by TBRC's market expertise and thousands of expert interviews conducted each year to verify the data.

The datasets on the global market model are created using a wide range of proprietary and public sources including leading government bodies, associations, trade journals, market intelligence reports and trade magazines. Data is modelled based on hard data, extrapolation, regression analysis based on known macro data inputs, interpolation between hard figures, comparisons with other geographies and markets, price estimations, and qualitative inputs. Data is triangulated within our unique market data model covering an exhaustive list of 600+ markets across 48 countries and 7 regions. Comparable data is used for sanity check and trend analysis. For example, our global market value data is compared to unit sales and price data for the relevant market as well as relevant macro-economic datasets in order to establish validity.

Market Numbers And Competitor Market Share

Market value of the animal testing market is estimated considering different parameters including the total revenues of major animal suppliers (animal breeder, CRO companies), the total number of animals being used per year in laboratory research, the average price of each animal, and the operational cost for each test in the USA, and China. The modeled market value numbers are validated by primary inputs.

The animal testing market is segmented by end use application into pharmaceuticals, academic research, medical devices, chemicals & pesticides, cosmetics, and others. The shares of these end use applications are obtained from primary interviews with industry experts in both the USA and China.

Market value of the non-animal alternative testing technologies market is estimated considering the total revenues of major alternative animal testing technology companies, the number of animal tests being replaced by alternative technologies, and the average price of alternative animal testing per test (different prices for different types of tests). Further the market is also estimated from the parent markets including the organ-on-chip (OOC) market, the in vitro testing market, the cell culture market among others. The modeled market value numbers are validated by primary inputs.

Analysis

Analysis is drawn from our Consultants' wide range of industry and research experience as well as public and proprietary sources. The Consultants are trained in research techniques and ethics by the Market Research Society.

Verification Through Expert Interviews

Every year The Business Research Company carries out thousands of interviews with senior executives and industry experts across hundreds of markets. Through these interviews, we develop our internal understanding of markets and geographies and cross reference our understanding of global markets with expert feedback utilizing 'Delphi' research methodologies.

Referencing

The Business Research Company prides itself on the quality and validity of its data and analysis. Our unique 'end noted' referencing approach allows the user to trace our market numbers and analysis back to the specific data sources they were derived from.

Note on Currency Conversions –

All currency conversions are carried out on the basis of 2018 exchange rates.

OCED Accepted In Vito Tests

The table below shows OECD accepted in-vitro tests for medical devices:

Table 9: OECD Accepted In-Vitro Tests For Medical Devices

Test Name	Use
TG 431	Skin Corrosion
TG 439	Skin Irritation
TG 441 C-E	Skin Sensitization
TG 428	Skin Absorption
TG 432	Pototoxicity
TG 437, 438, 460, 492	Eye Irritation

The Business Research Company
Source: Altex.org[clxxviii]

OECD have accepted more than 10 tests as non-animal alternative testing technologies for medical devices. But major regulatory agencies such as the FDA and EMA have not yet adopted these tests as an efficient replacement for animal testing for medical devices.

Survey on Animal Models & Testing Landscape in the US

Current Condition By Company

This section details about the number of animals tested by the major pharmaceutical companies, human resources required for animal experiments, location of animal testing facilities and average unit price of animal in the USA.

Number Of Animals Used In Testing

There are different types of animals used for testing in the laboratories across the world. The most common animals used for research purpose include mice, rats, guinea pigs, rabbits, fish, dogs, cats, birds, and farm animals. Major pharmaceutical companies that perform animal experiments are Novartis, Sanofi, GSK, AstraZeneca, and Bayer.
The companies or the research facilities that use animals for scientific studies generally breed their own stock specifically for rodents, rabbits, and birds whereas other animals such as pigs and sheep are obtained from farmers.[clxxix]

The table below shows the number of animals tested by major pharmaceutical companies globally.

Table 10: Number Of Animals Tested Globally in 2018

S.No.	Company	Number of animals tested
1	Novartis	512,137
2	Sanofi	410,867
3	AstraZeneca	121,823
4	GSK	231,000
5	Bayer	102,515
6	Novo Nordisk	~50,000

The Business Research Company
Source: TBRC Secondary[clxxx, clxxxi, clxxxii, clxxxiii]

The number of animals tested by the major pharmaceutical companies globally ranges from 0.05 million-0.5 million. Among the number of animals tested globally by the major pharma companies, 50% of the animal testing is done in the USA alone. Pharmaceutical companies primarily use rodents out of which mice is mostly preferred.

"Of the global volume of animals tested by AstraZeneca, around 50% of the animals are tested in the USA. The similar trend is seen by other major pharma companies as well."

- Environmental compliance and sustainability personnel, AstraZeneca, USA

"Number of animals tested by our company per year may be around 40,000 globally."

- Research Scientist, Bristol Myers Squibb, Former employee of Covance, USA

"Number of animals tested by our company at my location per year may be around 1,000. Overall estimation would be very hard to tell."

- Facility Manager, NAMSA, USA

"I'm not sure on the exact number of total animals. However, it would be around 1,500 mice per annum at my lab."

- Animal Care Technician, Genentech Biotechnology (A Roche Company)

"A range of around 500-600 animals are tested annually as we are small pharma company."

- Preclinical Scientist II, Lyra Therapeutics

Human Resources Required For Experiments

Animal research facility consists of scientists and laboratory animal care workers who are involved in the research process. Scientists perform research studies on animals to understand their behavior and intelligence. Laboratory animal care workers include assistant laboratory technicians, laboratory animal technicians, and laboratory animal technologists who help scientists in their animal experiments.

The average number of human resources required for conducting animal experiments in a laboratory is around 30-50. In order to perform animal experiments, scientists spend around two hours and the remaining workers who are involved in ensuring the food, water and cage for animals spend around 4-5 hours per day in their facilities. Some non-farm animal caretakers also work part time.[clxxxiv]

"Technicians work under scientists generally in the laboratories. So, approximately in our center 30 to 40 people (including technicians and scientists) are involved in the animal testing. Each technician tends to work with scientist. Scientists spend around 2 and half hours on animal testing and rest of the time they spend on conducting other multiple studies. Sometimes, one technician may work with two scientists. In that case, the technician works for around 2 to 2 and half hours in the morning and 2 and half hours in the evening.

If there is a big study, then multiple technicians work doing multiple things such as collecting samples and certain body parts.

- Environmental compliance and sustainability personnel, AstraZeneca, USA

"On an average, a facility would have 30-40 technicians working on the ground level providing care to the animal. Next to or below them there would be around 20 sanitization technicians who clean the equipment, cages, etc. Above the animal technicians, there would be scientific researchers, who might be around 20-30 in number. Each person would be working 8 hours a day. These personnel don't include administration/management people."

- Animal Care Technician, Genentech Biotechnology (A Roche Company), USA

"Number of human resources in the University of Nebraska (to which I am associated with) is around 100 people. These hundred people include people involved in taking care of animals, changing cages, technicians and scientists.

In our company (out of 3 facilities, animal testing is done in 2 facilities), around 50 people are working in each facility and total number of hours spent is 4 hours per day."

- Research Scientist, Bristol Myers Squibb, Former employee of Covance, USA

"At any given facility, human resources varies with the size and infrastructure of the organization. Number of people working in pre-clinical research ranges from 10-200."

- Associate Director, UT Southwestern Medical Center (Animal Resource Center), USA

"In our facility, there are around 40 people involved in animal testing. They would be working for around 3-4 hours for animal testing and the rest of the time they would do documentation or other works."

- Associate Director, UT Southwestern Medical Center (Animal Resource Center), USA

Location Of Animal Testing Facilities

The research and development facilities for the major biopharma companies in the United States are around 5 to 6. However, not all these research facilities may be involved in the animal testing. Therefore, as per the TBRC Analysis, the average number of research facilities in which the animal experiments are conducted is three in the United States.

"We have 2 research facilities in the USA. Ours is the main location. More animal experiments are conducted in our facility than the other facility."

- Environmental compliance and sustainability personnel, AstraZeneca, USA

"In our company, out of 3 research and development facilities, animal testing is done only in 2 facilities."

- Research Scientist, Bristol Myers Squibb, Former employee of Covance, USA

"Our company is in couple of different locations. In the United States, we have two research and development facilities where we perform animal experiments, one in Sacramento California and the other in Connecticut."

-Technical Information Scientist, Jackson Laboratories, USA

Average Unit Price

The widely used laboratory animals for scientific research are mice, rats, guinea pigs, rabbits and non-human primates (monkeys). Among these laboratory animals, mice are mostly used for research. The average cost of mice ranges from $20 (basic model)-$300 (transgenic).

"It depends on the kind of mouse we use. Lot of lab bred mouse are going to be more expensive. Range is 10 or 20$ to 300$. This range is followed throughout other pharmaceutical companies. Transgenic mice that are genetically modified are expensive. White mice are cheaper."

- Environmental compliance and sustainability personnel, AstraZeneca, USA

"It depends on the type of mice that we are using. Transgenic mice are expensive.Price of mice is 8 to 10$ for the basic models and more than $200 for expensive models but 90% of the animal testing is done by cheaper mice. Average cost of monkeys can be more than $1000."

- Research Scientist, Bristol Myers Squibb, Former employee of Covance, USA

"The price of rodents ranges from - $12 to $400 and rabbits - $250

- Associate Director, UT Southwestern Medical Center (Animal Resource Center), USA

"Rodents– around $10, Swine - $227 to 1,000 (price varies with the specialized breed. For Example, a mini pig cost around 1,000), Transgenic animals are twice as much as non-transgenic ones. Rabbit – About $125."

- Facility Manager, NAMSA, USA

"The price can vary depending on the type of mouse. The cheaper mouse can be around $20 and the expensive ones can go along $300.

Lot of animal models that are used are the inbred mice models meaning that they have consistent genetics. The more expensive mice have specific modifications like mutations, gene knockouts. These are genetically modified to have certain characteristics."

- Technical Information Scientist, Jackson Laboratories

"We use rodents and rabbits and the price of rodents range from $8 to $200."

- Preclinical Scientist II, Lyra Therapeutics

Expert Interviews List

Table 11: Expert Interviews List

S.No	Designation	Company	Location
1	Chief Scientific Officer	In-Silico Biosciences Inc.	USA
2	Senior Research Fellow	Harvard Medical School & Wyss Institute	USA
3	Business Development Manager	Emulate Inc	USA
4	Post-Doctoral Fellow	Swarthmore College	USA
5	Senior Preclinical Researcher	Boston Scientific	USA
6	Manager, Preclinical Genomic Services	Reprocell, USA	USA
7	VP-Business Development	TissUse Gmbh	Germany
8	Director	Center for Comparative Medicine at Baylor College of Medicine	USA
9	Senior Scientist	Applied BioMath	USA
10	Sales and Marketing personal	J-TEC (Fujifilm)	China
11	Preclinical Research Support Division Manager	Shin Nippon Medical Laboratories Ltd.	China
12	Professor	Laboratory of Laboratory Animal Science and Medicine, Hokkaido University	China
13	Director	Astellas Pharma	China
14	Professor & CEO	Kyushu University & O'Atari Inc	China
15	Professor	Laboratory of Molecular Pharmacokinetics, University of Tokyo	China
16	Environmental compliance and sustainability personnel	AstrZeneca	USA
17	Research Scientist	Bristol Myers Squibb	USA
18	Associate Director	Animal Resource Center, UT Southwestern Medical Center	USA
19	Facility Manager	NAMSA	USA
20	Technical Information Scientist	Jackson Laboratories	USA
21	Executive Director	Stop Animal Exploitation Now (A non-profit animal care organization)	USA
22	Animal Care Technician	Genentech	USA
23	Preclinical Scientist II	Lyra Therapeutics	USA
The Business Research Company			

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