Animal Welfare Report 2021

Association of research-based pharmaceutical companies

interpharma:ph

Content

Foreword

Rarely before has medical research received as much attention as it has in the past year. Not a day passed without the media reporting on developments in the diagnosis, prevention and treatment of Covid-19. During this period marked by high expectations, pharma companies responded to this crisis together with scientific institutions and regulatory authorities in a wide variety of countries. Various test methods and vaccines were produced in record time, and companies also pressed ahead with the development of therapies and medicines. But what is often forgotten is that the development of new substances already begins before the first clinical phase and applications for regulatory approval. In basic research, animal experiments are used to understand the disease and its progression in the first place. In the subsequent preclinical research, among other things, the efficacy and safety of potential drug candidates are investigated in preparation for the clinical phase.

To ensure that medical research in animals is approached ethically, the research-based pharmaceutical industry in Switzerland introduced its 10-point charter back in 2010. The aim of the charter is to improve the protection and welfare of laboratory animals in the breeding and housing of animals and in the necessary experiments. Interpharma members are guided here by the principles of the 3Rs: alternatives to animal experiments are used where possible (Replace), the number of laboratory animals is scaled down (Reduce) and any stress on the animals is kept to a minimum (Refine). The Animal Welfare Report 2021 illustrates how our members are applying the 3Rs for the improvement of animal welfare. This year's edition shows how the Culture of Care is changing the research-based pharmaceutical industry. Culture of Care takes a holistic view of the appreciation, resilience and well-being of humans and animals. It follows the principle that animal welfare and the appreciation of employees are correlated: companies that appreciate their employees, involve them in decisions and processes and integrate them reach better animal welfare. This is noticeable both in the strategy and culture of the company and also in the practical aspects of structural measures or design of research projects. Animal welfare is no longer just a sideshow – it is established in the corporate decisions of our member companies. The lived Culture of Care in animal welfare concerns everyone who has any influence on the well-being of animals. This goes for everyone from management, which establishes the framework conditions, to the animal keepers and researchers who have direct contact with the animals.

Dr. René Buholzer
CEO Interpharma

The Animal Welfare Report 2021 also takes up the discussion around the introduction of a ban on animal experiments in the Netherlands. In the meantime, the ban has been lifted because the fears of researchers proved to be well-founded: without animal experiments medical progress under ethical conditions is not possible. In this discussion, it was argued that all animal experiments already today can be replaced by alternatives without jeopardizing the safety of patients. This is not the case: without animal experiments there would be no new, safe and effective medicines for serious diseases such as cancer and multiple sclerosis or vaccines against viruses such as SARS-CoV-2. Rather than further restrictions on animal experiments, therefore, the principles of the 3Rs and the motto "control instead of bans" must continue to be followed systematically. They enable Switzerland to maintain its place as an innovative research hub and ensure that patients can be supplied with vital medicines.

Development of vaccines and tests for SARS-CoV-2

Just a year after the outbreak of the pandemic, various highly effective vaccines were already available. The first highly automated coronavirus tests also allowed test capacity to be ramped up early on. Without the responsible use of animals this would not have been possible.

Rapid test infrastructure and vaccine development
While the pandemic still seemed a long way off in Switzerland, researchers in Germany already developed the first test infrastructure for SARS-CoV-2 in January 2020. It took a few more weeks before the first wave of the virus swept across Europe. And in March, a market-ready test was already available from Roche. The test technology has since seen rapid improvements – testing for Covid-19 today is cheap, less invasive and also reliable. It took just one year before effective vaccines became available: the first effective vaccines were available at the end of 2020 and thus only twelve months after the pathogen was identified at the end of 2019. Usually, it takes between six and fifteen years from development through regulatory approval to market launch of a vaccine.

Reasons for the rapid progress
The rapid provision of test facilities and vaccines for SARS-CoV-2 can be attributed to three main factors. Firstly, the research community had already spent thirty years working on the mRNA technology that forms the methodological basis of various vaccines for the coronavirus; they were also able to fall back on other technical approaches and experiences. Secondly, there was a unique international collaboration between science, pharmaceutical companies and biotech start-ups. The various synergies that arose from this made rapid scientific advances possible. And thirdly, the regulatory authorities of various countries allowed a fast-track approval procedure. In addition to the key factors, basic research forms the cornerstone for all medical research. No medicines or therapies can be developed without exploratory university research which is conducted without any expectation of results and is also dependent on the use of animal experiments. A crucial element of medical research on substances is always the measurement of their safety and efficacy. Animal experiments are an indispensable method of testing these two factors – also in the case of vaccines and tests for SARS-CoV-2.

Research on mRNA goes back 30 years
Messenger RNA vaccines were discovered and developed over the last thirty years. Synthetically produced RNA is introduced to the cells of the body by inoculation. This RNA provides the cells with the blueprint for proteins which in turn trigger an immune response against the virus. RNA that enters a cell carrying information for producing proteins is called messenger RNA – hence the abbreviation mRNA. In the early 1990s, the Hungarian scientist Katalin Kariko carried out pioneering work on the development of therapeutic approaches using mRNA. Following a search for research funds that was initially fraught with problems, she succeeded in discovering a functioning immune response with the aid of synthetic mRNA together with research colleague Drew Weissman in the USA.

"Many years of experience working with mRNA allowed rapid progress to be made in research."

Joachim Coenen
Expert Animal Science and Welfare
Corporate Animal Science & Welfare at Merck KGaA

12 months

It took only twelve months from discovery of the virus to the first market-ready vaccine.

After her university career, Kariko continued the research at BioNTech. Her team was originally focused on vaccines against cancer, where mRNA specific for the occurrence of a cancer is produced for patients. But when the pandemic started, BioNTech and its partner Pfizer concentrated on the development of a vaccine against SARS-CoV-2. Instead of developing everything from scratch, BioNTech looked for the correct mRNA sequence for the production of a protein that triggers an immune reaction to the virus.

International collaboration
This rapid development of different vaccines is an extraordinary achievement that was made possible by an unparalleled international collaboration on all levels. Research-based companies had already gathered initial experience of dealing with coronaviruses with SARS-CoV-1 in the early 2000s – and MERS in 2012. As a consequence, the genetic code of the virus in the Covid-19 pandemic was deciphered early on. On thebasis of the information available, various companies were able to begin work on the development of a vaccine. The collaboration between academic institutions and the pharmaceutical industry also served to accelerate vaccine development.

AstraZeneca, for example, developed a vector vaccine together with the University of Oxford. Successful cooperation between companies also had an impact: Pfizer developed an mRNA vaccine in collaboration with the German biotech company BioNTech. Johnson & Johnson developed a DNA vaccine using vectors in collaboration with its subsidiary company Janssen and its vaccines site in Bern. This vaccine, too, involves a new technology, which has already proved successful in vaccination against Ebola. With Lonza as a new production partner, Moderna was able to achieve a tenfold increase in the production capacity for its vaccines. As a result of this cooperation, Lonza in turn its expanding its facilities in Visp (VS).

Openness and flexibility of authorities
Aside from various forms of cooperation, accelerated and simplified procedures in the clinical phase also helped to speed up the review processes for the efficacy and safety of vaccines. Thanks to their openness to fast-track procedures, the authorities helped to ensure that the first vaccines were approved in record time. Despite the great urgency, safety (and efficacy) had and still have utmost priority. But producers were able to have various development processes running in parallel. This way, for example, different clinical trial phases could be combined. Pharmaceutical companies also recruited trial subjects simultaneously for different clinical trial phases. If one avenue of research proved unsuccessful, costly later clinical trial phases would have been redundant. The sharing of information between regulatory authorities was also stepped up and the approval process of Swissmedic was accelerated. Normally, the results of clinical phases I–III are collected and reviewed as part of the approval procedure. For an approval of vaccines against the coronavirus, however, individual studies were submitted to Swissmedic and reviewed in a rolling process. This delays in the process were avoided without any shortcuts when it came to safety.

The 30 years of experience in working with mRNA technology, the unparalleled international collaboration between the scientific community, pharmaceutical companies and biotech start-ups as well as the acceleration of regulatory procedures by the various authorities enabled vaccines to be developed in record time. But the pandemic has also shown us that, without the responsible use of animals, this would not have been possible.

From basic research to market readiness

1 Basic research

Thousands of substances

Development of vaccine technologies
Decades in the development of mRNA, DNA vector and virus protein vaccines

Search for target molecules
Search for molecules and lead structures in molecule libraries

Drug design, synthesis and effect
In biochemical experiments, cell systems and using computer-aided processes

2 Preclinical research

1 

Analysis of the virus
What is it that triggers immune responses?

2 

Vaccine design
What part of the virus and which auxiliary substances should be included?

3 

Testing in animals
Efficacy, tolerability

3 Clinical research

1 

First testing in humans
Testing tolerability in approx. 10–100 human subjects

2 

Clinical trials
Testing efficacy in approx. 100–500 human subjects

3 

Further clinical trials
Evidence of treatment success in > 20,000 human subjects

4 Approval and market launch

1 **Application to Swissmedic for approval**
Experts review all the study data generated.

2 **Application to FOPH for reimbursement**

1 million

About one million different substances are considered in the research for a single drug.

Basic research is the cornerstone of all medical research
The production of vaccines in such a short space of time requires in-depth prior knowledge of countless molecules, substances and compounds. This is where basic research comes in. Basic research is not aimed at the development of a marketable product and remains open as to the results. Researchers are not looking for a specific property, but are interested in any effects. The substances studied provide the cornerstone for medical research. Of the countless substances that emerge from basic research, few make it to preclinical studies and clinical trials. Research on vaccines against SARS-CoV-2 thus began a long time before the virus was first reported. In the search for the right substance to combat the coronavirus, research teams fell back on substances investigated in the course of basic research. Every vaccine is based on tests with thousands of substances of which barely a few dozen were considered for the shortlist. This process is all part of preclinical testing.

Preclinical testing of safety and efficacy
There are primarily two criteria for exclusion that researchers apply to reduce the number of substances: efficacy and safety. Measuring these is a complex matter: the methodology ranges from computer simulations through testing with bacteria, cell and tissue cultures to tests in isolated organs. When all other avenues for testing have been exhausted, animal experiments are used. Every study involving animals must be approved by the cantonal veterinary authorities, who refer to the recommendations of the independent cantonal committees for animal experiments before deciding whether to grant approval, often with conditions, or not. For the protection of patients against serious side effects, animal experiments are required by law, before any clinical trials can be conducted. These regulatory animal experiments allow researchers to establish whether a substance is toxic and how long and how potent its effect is. A toxic substance can trigger diseases or cause genetic damage. From an ethical standpoint, therefore, a risk of this kind is unacceptable in the treatment of humans. The efficacy of vaccines is measured on the basis of the antibodies produced. Since current technology is not able to simulate an immune response in vitro – i.e. in a test tube – researchers must still resort to animal experiments for this, as animal experiments allow interactions of a substance to be studied in live organisms.

For medical progress
Without preclinical testing in animals, research into new medicinal substances would thus be unethical towards the human subjects in the subsequent clinical trial phases. The rejection of research using animals therefore prevents medical progress. However, researchers also have an ethical obligation with regard to the well-being of the animals. For this reason, pharmaceutical companies and scientific institutions in Switzerland follow the 3Rs strategy. In view of the incredible medical advances of the last few years, there can be no question of forgoing animal experiments: otherwise we would not have any vaccines now against the coronavirus nor effective therapies for cardiovascular disease, various forms of cancer and other serious diseases.

"Coronavirus vaccines would never have been approved without animal experiments."

What has the pharmaceutical industry done to help beat the pandemic?

RB: The research-based pharmaceutical industry has contributed enormously in the engagement against the pandemic. On the one hand, companies diverted research and development resources in short order, allowing research to be pursued on various vaccines against SARS-CoV-2, with the result that the population was fully supplied with vaccines. Their regular contact with the Swiss government provided for an efficient regulatory approval process. At the same time, the pharmaceutical companies ensured that drug supplies and patient safety in Switzerland were secure at all times. The scarcity of resources was particularly challenging and hampered the transportation capacity that arose as a result of the pandemic. The numerous cooperative efforts with academic institutes were also very positive.

What role do animal experiments play in the development of medicines and vaccines for Covid-19?

They play an essential role, because the regulatory conditions for the approval of a vaccine are internationally harmonized and specify that testing in animals is required. In March 2020, the twenty most important regulatory authorities agreed on the data that needs to be gathered for approval. It should be pointed out here that the safety-relevant tests in fast-track procedures for the approval of vaccines were and are never reduced to gain time. Animals were used in a two-tier system of testing. Before clinical trials were conducted, vaccines were tested in both rats and mice. In these initial preclinical animal studies, the researchers sought to establish whether an immune response is triggered and what the optimum quantity and frequency of vaccine dosing is. Scientists then tested the vaccines also in rhesus monkeys, because human-like symptoms such as pneumonia can also occur in these animals. For reasons of transparency, the results of preclinical studies are made publicly accessible. Animal experiments are both required by law and ethically mandatory for the protection of humans. Coronavirus vaccines such as those from Moderna and BioNTech/Pfizer would never have been approved without animal experiments.

What have Interpharma and its members learned from experiences in the pandemic?

The global race to develop an effective vaccine has resulted in a boost to research, especially in the field of betacoronaviruses and viral infectious diseases. The rolling approval procedures in the pandemic highlight the possibilities for the reform of regulatory approval processes, because delayed approval primarily results in poorer patient access to innovation. Pharmaceutical companies are also dependent on low international trade barriers and hence open borders. As a result of the severe shutdown in some economies and industries, global procurement and supply chain management are particularly challenging for the pharmaceutical industry. In Switzerland, they are dependent in turn on the country's position as an attractive research and business hub.

"The focus is always on patient safety."

Switzerland must safeguard its attractiveness in the longer term – this includes favourable framework conditions for taxation, easy access to qualified specialists and active support for innovation and start-ups. The research-based pharmaceutical industry is also prepared to help drive digitalization together with the federal government and other actors involved in the healthcare system, because good-quality anonymized health data provides for a faster and more precise development of medicines and therapies. And this will be essential in the coming years for Switzerland's position as a leading research hub.

Culture of Care

Today, the pharmaceutical industry thinks holistically about well-being in medical research: animal welfare and a caring corporate culture go hand in hand.

It concerns everyone

For years, research-based pharmaceutical companies have striven to improve animal welfare in research. At the same time, the employees, managers and corporate management in the entire organization must not be neglected. A Culture of Care therefore takes a holistic view of appreciation, resilience and well-being of animals and humans alike. The Culture of Care must be deeply embedded in the corporate culture. Ideally, it is reflected in all business activities. The lived Culture of Care in the field of animal welfare concerns everyone who has any influence on the well-being of animals. This goes for everyone from management, which establishes the framework conditions, to the animal keepers and researchers who have direct contact with the animals. It also concerns the workshops that maintain the facilities and other parts of the organization which, at first glance, appear to have nothing at all to do with in vivo research.

The five pillars

A Culture of Care can be seen as a culture built on five pillars. The corporate values form the first pillar in the Culture of Care, which requires a corporate policy that delineates the way in which responsible animal research is conducted; it should regard animal protection and care as a priority and support transparency in relation to animal experimentation activities both internally and externally. This requires a strategic approach as the second pillar: first of all, management provides corporate directions concerning the Culture of Care and empowers the employees who work with animals; for this, management determines the relevant roles in the company and assigns responsibility.

In practice

The next pillar is the establishment of clear structures that support the Culture of Care and make it possible. Personnel support forms the fourth pillar. Every institution has a local management that supports and furthers the change. It has a responsibility to the employees for the demonstration of care and engagement. This leads to the pillar of practical work. In animal care, the company develops processes that foster continual improvement in the 3Rs. The use of animals involves appropriate planning of experiments and a refinement of care and animal welfare practices.

"Including employees in care ideas also helps the well-being of the animals."

Dr. Birgit Ledermann
Novartis 3Rs Leader,
Novartis Institutes for BioMedical Research

Ethical dimensions of the Culture of Care

The ethics of care described by political scientist Joan Tonto shows the ethical dimensions that are served by a Culture of Care.

1. Responsibility: for cultural, ethical and legal reasons, the research community is responsible for looking after animal welfare.
2. Attentiveness: employees and management must be aware of and appreciate the needs of their colleagues and of research animals.
3. Competence: research institutions are responsible for establishing competence so that advances in animal welfare can actually be achieved – without diminishing the quality of the research.
4. Responsiveness: the biggest ethical challenge of research using animals is to establish an empathy for all those involved that still allows medical advances to be achieved.

Ethical and entrepreneurial

Providing information throughout an organization and permanently raising awareness feeds the pulse that keeps the Culture of Care alive. If it is sustainably implemented, it forms a process that is perpetually driven, pursued and never completed. In this way, processes are constantly questioned and developed further. It benefits animal welfare if state-of-the-art technologies are used that yield better data and improve understanding for the needs of the animals. Viewed in this way, Culture of Care acts on two different levels: on the one hand, it facilitates strong corporate governance and an ethical framework for work; on the other, it has a positive effect on corporate results, allowing better experiments, which lead to more reliable and more effective medicines.

What does it look like in practice?

So-called tunnel handling serves as a practical example to explain Culture of Care. Whereas animal attendants, lab technicians and researchers did not often share ideas in the past, companies today encourage them to communicate with each other. This exchange of ideas led the research community to appreciate how much the way in which mice and other laboratory animals are lifted out of their cages or enclosures counts towards the care of the animals. “Tunnel handling” reduces the stress level of the laboratory animals, which leads not only to better test results, but also to greater animal well-being. At the same time, the change of culture has shown all employees that management takes their arguments and suggestions for change seriously.

The five pillars of the Culture of Care

Culture of Care

1	2	3	4	5
				
Values	**Strategy**	**Structure**	**Support**	**Practice**
Corporate policy as a guide	Corporate direction	Distribution of roles in the company	Implementation of care and engagement	Continuous improvement in the 3Rs
Prioritization of animal welfare	Definition of fields of action	Allocation of responsibilities	On-site management	Refinement of care and animal welfare practices
External and internal communication		Structural planning	Openness to improvement	Appropriate planning of experiments

Animal welfare

"The lived Culture of Care in animal welfare concerns everyone."

What is the influence of the Culture of Care on corporate decisions at Roche?

TS: We are aware that the use of animals in medical research comes with huge responsibility. We take the concerns around animal experiments in medical research very seriously and are committed to handling animals in a responsible manner. Everyone who works with animals at Roche or on behalf of Roche is committed to treating the animals entrusted to them with respect. We inspect all our service providers regularly before and during the collaboration and ensure that they are committed to complying with Roche standards. Culture of Care is a central factor in corporate decisions involving in vivo research. We offer the best possible conditions both to the animals entrusted to our care and also to our employees. This holistic view characterizes the Culture of Care. Our management sets the framework conditions for an innovative work environment and contributes significantly to the further development of animal welfare.

What does the well-being of staff have to do with animal welfare?

Our employees and animal welfare guide our considerations at all times. One example of this is the new in vivo research facility, Building 098. This building offers attractive working conditions – an ultramodern environment for both animals and humans, where innovation is made possible and fostered. It symbolizes the commitment of Roche and our employees to the Culture of Care as it is lived. The new research facility is completely digital and allows countless research parameters to be gathered online. At the same time, it protects the health of our employees: cages are automatically cleaned and replenished, which reduces allergic reactions among the staff. Mobile robots manoeuvre heavy loads, reducing physical stresses and strains. Our experience in Building 098 shows that appreciated staff are mindful of animal welfare – a high level of animal welfare reduces the burden on staff.

Did you have to suspend research operations during the pandemic?

The pandemic has tested our processes. For all our animal facilities we maintain "disaster plans" that describe in minute detail how we maintain a high-quality and ethical animal housing system during a disaster. This helped us a lot with the coronavirus crisis – we were prepared. We could therefore ensure that the animals were adequately cared for and monitored at all times. We immediately changed our modus operandi: in consultation with breeding facilities, we procured animals with modified priority and abstained where procurement was not necessary.

> "Both the commitment of all employees and management as well as investments by the company are indispensable in order to extend the Culture of Care. It's impossible without both elements!"

We also ensured that ongoing experiments were adequately monitored in order to prevent the unnecessary use of animals. And we protected our employees by allocating them to smaller groups. In this way, we always had sufficient qualified staff available – even if individual groups had to isolate because of illness. We thus maintained the Culture of Care at the accustomed standard without negative effects. We are proud of the fact that we were able to keep the animal facility and research operations going.

245 million

Investment in the new in vivo research facility Building 098 by Roche ran to CHF 245 million.

How did you deal with the difficulties of the pandemic?
The pandemic presented a particularly extreme situation for Roche as well. We focused our attention on our employees and together tried to get through this challenging time as well as possible. To this end, we provided them with support in setting up facilities to work from home or offered programmes to improve mental and physical well-being.

What is important, is that even under the exceptional conditions of the pandemic, our employees never lose their passion and hence their sense of the need for animal welfare. We countered the possibility of such empathy fatigue through careful management of the animal stock at the sites. As a result, the workload for our colleagues remained within easily manageable limits and we successfully avoided chronic overload and associated signs of fatigue. Nevertheless, the pandemic was and still is challenging – we are looking forward to a step-by-step return to normality.

What next with the Culture of Care at Roche?
The lived Culture of Care in animal welfare concerns everyone. Both the commitment of all employees and management as well as investments by the company are essential for extending the Culture of Care. It is not possible without both these elements! The culture is lived top down by management and deeply embedded in the consciousness of our employees, who live the culture in their day-to-day practice. Our investments in the Culture of Care underpin our aspirations. Both components show that we are sustainably and seriously striving for change. Let me describe an example: we sponsor Roche "3Rs Awards" worldwide, which we have been conferring every two years since 2008. With this award, we are raising awareness of the 3Rs principles, stimulating dialogue on the issue among employees and promoting research on alternatives to animal experiments. The sustainable implementation of a Culture of Care is a process that can never end, but must be constantly advanced and developed further. We need to keep questioning our processes and developing them further.
Only in this way can animal welfare be continuously improved.

"We require everyone who works with animals within Roche or on behalf of Roche to treat the animals entrusted to them with respect."

Dr. Tobias Schnitzer
Global Head of Comparative Pharmacology & Toxicology, Roche

In the 10-point Animal Welfare Charter, the Interpharma member companies commit to:

1 apply and actively promote the 3Rs (reduction, refinement and replacement of animal studies), especially with regard to the research, development and implementation of methods and techniques which allow further replacement of animal studies, a reduction in the number of animals used or alleviation of the pain and stress of laboratory animals.

2 ensure high-quality and state-of-the-art housing and care conditions for our laboratory animals and strive to continuously improve these conditions.

3 develop and foster education and training for all our employees and associates who work with animals.

4 contractually oblige external partners to comply with our high standards of animal welfare when they conduct animal studies for us or supply us with animals.

5 apply vigorous internal auditing systems, which ensure compliance with the animal welfare standards agreed upon.

6 joint efforts in auditing our external partners on animal welfare standards and compliance on a global level.

7 promote, in addition to regular authority inspections, the development of external, independent assessment programmes of our animal welfare standards and facilities on a global level.

8 promote the validation and regulatory acceptance of methods which are suited to the replacement, reduction or refinement of animal studies.

The 10-point Animal Welfare Charter was initiated in 2010 by Interpharma member companies. The aim of the charter is continually to improve the protection and well-being of laboratory animals during breeding, in the housing facility and during the necessary animal experiments.

9 contribute to a continuous, open and constructive dialogue on animal research and welfare with the public at large as well as with authorities, policymakers and other interested stakeholders.

10 report annually on the progress made with regard to this charter.

Dutch ban on animal experiments

In 2016, the Netherlands considered a complete ban on animal experiments by 2025. The plan was rejected: it is not possible without animal experiments.

The Netherlands planned to exit animal studies
In 2016, the Netherlands National Committee for the protection of animals used for scientific purposes (NCad) published a recommendation to transition to research without the use of animal experiments. It called for a gradual reduction and planned exit by 2025, particularly for animal experiments in the context of regulatory safety testing, i.e. safety tests required by law for chemical, foodstuffs, ingredients, pesticides and medical devices and vaccines. In the aftermath of its publication, the recommendation by the NCad was repeatedly cited as a "masterplan" to stop animal experiments in the Netherlands – wrongly, as has emerged.

An exit is not practicable
The German science initiative "Tierversuche verstehen" addressed the NCad report in depth and analysed additional documents from Dutch ministries. It emerged from this analysis that an exit of research from the use of animal experiments in the Netherlands was neither planned nor possible. The Netherlands also abandoned the 2025 deadline for an exit in the regulatory domain completely. In scientific basic research, applied research and educational programmes, an absolute renunciation of animal experiments is now seen as impracticable also by the NCad. For without animal experiments, it is not possible to conduct research into the complex functions of the living organism and the interactions of the various human organs, and thus neither the dangers nor the effects of substances can be tested. The scientific community would therefore be prevented from finding answers to biomedical questions without endangering human lives.

A ban would be unethical and put safety standards at risk
In the event of a total ban on animal experiments, two scenarios are conceivable: either there would be an unacceptable fall in safety standards, because medical research in humans would be conducted without preclinical research, which would not be ethically acceptable; or, for the protection of human subjects in clinical trials, medical research would not be carried out and scientific progress would thus be prevented. The Netherlands recognized this dilemma and abandoned the project. The objective of a complete exit was diluted into an intention to promote alternative methods and animal-free innovations, which was absorbed into the 3Rs strategy, according to which pharmaceutical researchers use alternatives to as many animal experiments as possible (Replace), use fewer laboratory animals (Reduce) and keep any stress on the animals to a minimum (Refine). Owing to a lack of alternatives, however, a moratorium on animal experiments is no longer being considered.

Outsourcing to countries with lower standards
Innovative methods and technologies have the potential to take science further and allow the number of animal experiments to be reduced. Experts from different disciplines are collaborating to promote the sharing of knowledge with respect to innovations without recourse to animal experiments. Going it alone in the way the NCad proposed for the Netherlands with regard to the animal experiments required by regulatory authorities, carries considerable risks.

History of the 3Rs

The 3Rs – Replacement, Reduction and Refinement – have their origin in the work "Principles of Humane Experimental Technique" by W. M. S. Russell and R. L. Burch. Before this, in 1954, the Universities Federation for Animal Welfare in the UK had launched a sponsorship programme for the development of ethical methods in research with animals. Two years later, the two researchers reported their first results to the foundation council, whereupon this book, which still points the way for animal welfare today, was commissioned. While some countries have written the principles of the 3Rs into their regulatory requirements, the Interpharma member companies committed voluntarily to the application and promotion of these principles more than ten years ago.

While research in the Netherlands (as also in Switzerland) is conducted at the highest ethical level, for example, research processes in the event of a moratorium would be outsourced to countries with lower standards. This means that lower ethical requirements would be applied for the handling of animals and the safety of experiments. A ban on animal experiments in European countries would have the effect of lowering ethical standards in medical research overall. Strategies such as the 3Rs must therefore always be implemented in the international context.

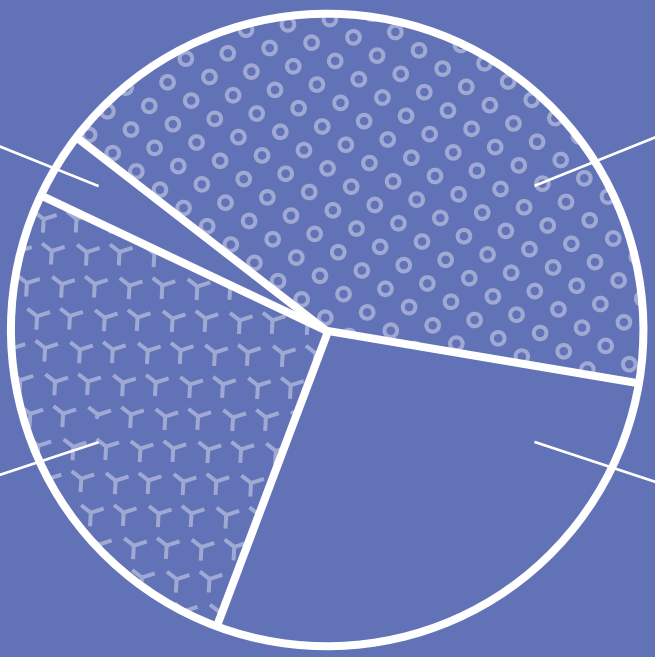
The 3Rs strategy points the way

The call for a ban on animal experiments is not new. Even in the peak phase of the first wave of the coronavirus pandemic, petitions were filed with the European Commission in March and April 2020 for a complete ban on animal experiments. One of the arguments put forward by the petitioners to justify this move was that the Netherlands already had a timetable for the abolition of animal experiments. But what the research community had already suspected in the formulation of the exit plan was later confirmed politically: there is no longer any concrete plan in the Netherlands today for abolishing animal experiments. As shown for example by the SARS-CoV-2 pandemic, animal experiments are essential for research into life-saving therapies or vaccines. And in regulatory safety testing, too, it is only possible to manage without animal experiments if validated, internationally recognized alternatives are available. There can be no binding exit plan for abandoning animal experiments in the foreseeable future, and this is due to the lack of alternatives – not to the lack of will on the part of the research community. In conclusion, it has to be said that the systematic promotion and implementation of the 3Rs principles – Reduce, Replace, Refine – is the effective way to improve the quality of research and the welfare of the animals used.

Animal experiments in Switzerland in 2020

All animal experiments requiring approval that were conducted by hospitals, universities, ETH, industry, the federal government, cantons and other parties.

Severity



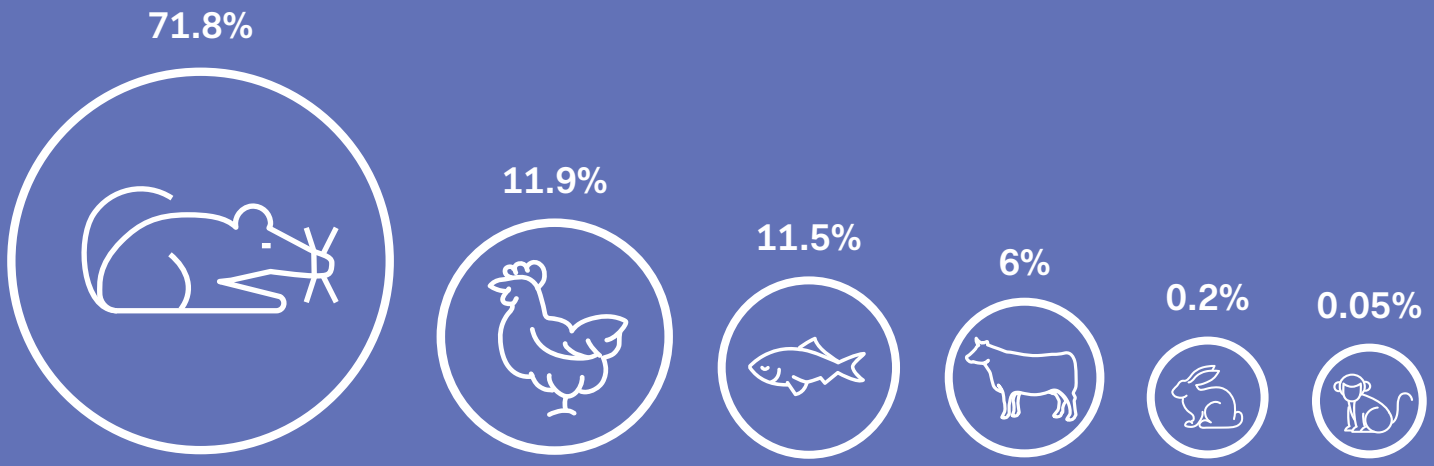
3.5%
Severity grade 3
19,712 lab animals

42.3%
Severity grade 0
235,280 lab animals

26.2%
Severity grade 2
145,551 lab animals

28%
Severity grade 1
155,564 lab animals

Animal species



71.8%
399,053
mice and rats

11.9%
66,242
birds
(incl. poultry)

11.5%
64,102
amphibians,
fish and reptiles

6%
23,562
bovines, horses,
donkeys, various
mammals

0.2%
1053
rabbits and
rodents

0.05%
190
primates

Source: Animal experimentation statistics, Federal Food Safety and Veterinary Office, 2021.

"We foster promotion of the 3Rs for better animal welfare in Switzerland."

Why did you decide to accept the position as director and what are your goals?
JS: I had already spent some years working in research management at the Swiss Centre for Applied Human Toxicology (SCAHT) and the vacancy as executive director of the 3RCC seemed ideal to me. The principle of the 3Rs was a central part of my earlier career as researcher – also in the research programmes that I had the privilege to develop at the SCAHT. What excites me at 3RCC is that I'm in a position to influence the research landscape in Switzerland. I want to achieve progress to the improvement of science and strengthening of animal welfare. The organization has a unique structure with a very diverse internal stakeholder group. My principal personal goals are steadily to expand on existing collaborative projects and find solutions with a broad impact.

How is the 3Rs strategy in Switzerland progressing?
Founding the 3RCC was an important step towards addressing the challenges of implementing the 3Rs in Switzerland more robustly. While the 3Rs Foundation funded many highquality research projects in the past, research alone is not enough – educational work and communication are just as important. The complexity of the nationally coordinated effort to promote the 3Rs needs our institution. We are learning from projects in other countries, such as the NC3Rs in the UK. This has now been successfully established, but it takes time and dedication to arrive at a point that is recognized as progress. With the engagement and passion of our board, I am confident that we can achieve a lot! Research in 2021 is completely different from research in 1959, when the principle of the 3Rs was first described. The aim of the 3RCC is to make the latest scientific trends and developments available in Switzerland.

Why are animals so important for medical research?
Although the level of knowledge among the global research community has grown enormously, we must retain a sense of modesty: we are also aware, after all, that there is an awful lot we do not know. All research models have their limits, and what counts in research is the scientific question that is posed. While we have certain technological options at our disposal to answer some questions using models that do not involve animal experiments, some questions are just too complex to resolve with research models that dispense with the use of animals. The complexity of the live organism can often not be adequately replicated by artificial means. Especially since animals play an important part in biomedical research today, we are searching tirelessly for alternatives to animal experiments. For this reason we are steadily encouraging and promoting the development of new, complex methods, such as organoids and multi-organ-on-a-chip technologies.

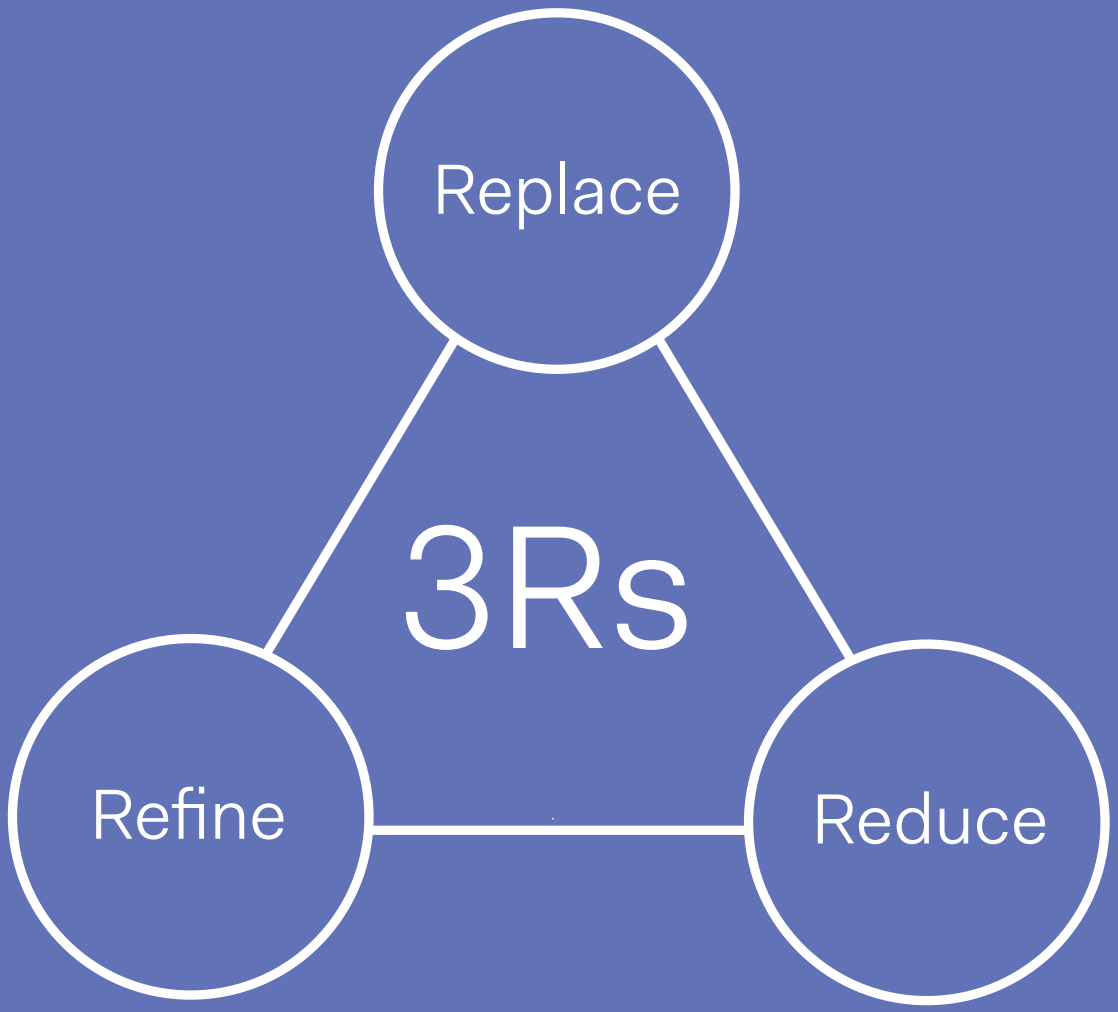
"Some questions are just too complex to resolve with research models that dispense with the use of animals."

So, is the 3RCC aiming to cease research with animals?
We have to reflect on the principle of the 3Rs – replace whenever possible and, if not, reduce the number of experiments and the level of stress to a minimum. Technological progress will steadily widen the options for replacement. Our aim is to promote the 3Rs for better animal welfare and a better quality of science in Switzerland by changing the mindset, ensuring good 3Rs practice and building networks for science. I will always stand up for a strict application of the principle of the 3Rs. A ban on animal experiments, however, is not part of this agenda. Doing without animal experiments entirely is not possible today, and nor will it be in the coming decades.

Jenny Sandström
Executive Director,
Swiss 3R Competence Centre

Published for the first time in 1959, the principles of the 3Rs today are widen in both national and international law on animal welfare.

Live and sentient laboratory animals should be replaced as far as possible by non-sentient material such as cell models.



The laboratory animals used are treated as gently as possible. This relates to the entire life of the animal: breeding, transport, housing, experiment and, where applicable, also euthanasia.

The objective of the experiment should be achieved with as few animals as possible.

Promotion of the 3Rs

The aim of the 3Rs principles is to Replace as many animal experiments as possible, to Reduce the number of laboratory animals used and to keep stress to a minimum (Refine).

Animal Welfare Strategy
Both from an ethical and from a scientific standpoint, animal experiments for medical purposes are required by law to ensure patient safety. It goes without saying in this regard that our members always act in keeping with all applicable laws and regulations. To make sure compliance with the highest ethical standards is improved even further, an Interpharma member has developed a new animal welfare strategy, the aim of which consists in defining binding rules throughout the company for the use of laboratory animals. This includes the implementation of efficient organizational structures and the definition of specific key performance indicators (KPIs).

To boost the animal welfare approach, a newly developed governance structure has been introduced and a new organization established. The aim of these efforts is to achieve the overarching goal of replacing animal experiments with alternative methods, reducing their number and improving them. The member company concerned appoints at all its sites around the world where animals are kept animal welfare officers and laboratory animal experts with local responsibility, who report directly to the company's governance unit – regardless of the business. They serve as attorneys for the animals, and their mission is to ensure ongoing improvement in this field. A Global Animal Welfare Committee, which is chaired by the company's CEO and on which representatives of all business units have a seat, serves as a communications and implementation body.

What the new animal welfare approach means:
- The member company attaches great importance to the ethical principle of the 3Rs – Replace, Reduce and Refine – with regard to the use of laboratory animals.
- Moreover, the company has introduced a fourth R, namely Responsibility. Everyone in the company, as individual or as the member of a team, is called on to take responsibility for the animals or products of animal origin used, to show maximum respect for the animals and also for the colleagues who work with animals and play an active role in the development of alternative methods to the use of animals. In this context, a company-wide 4Rs programme has been developed, which brings together expertise from all areas of the organization in a collaborative effort to replace, reduce and improve the use of animals through innovative approaches and live up to our responsibility for all animals that are used on its behalf.
- Governance in the field of animal welfare and laboratory animal science and compliance specific to the area of research are organized on the basis of four thematic cornerstones: Animal Welfare, Animal-Using Vendor Management (governance of providers that use animals), Vivarium Oversight (governance of the company's in-house animal facilities) and the principle of the 4Rs.
- Providers that use or keep animals on behalf of the company must be regularly qualified and audited.
- Independent, multidisciplinary and verified company committees (Animal Usage Review Boards) will approve all work that involves the use of animals in-house and on behalf of the company.
- A new centralized IT tool is being implemented to facilitate and improve processes across all functions, to create transparency with respect to work with animals and to allow knowledge to be shared.
- A comprehensive, company-wide set of regulations is currently being drawn up for Animal Science & Welfare and organizational changes and processes are being implemented in support of businesses.

Animal Research Tomorrow

More than 4700 researchers have signed Animal Research Tomorrow (formerly The Basel Declaration) and committed to observe the 3Rs in biomedical research. The co-signatories are also promoting trust in research through increased transparency.

Project name:	Animal Welfare Strategy
Charter articles:	1, 2

Animal welfare has long ceased to be a sideshow – it is now established in the corporate decisions of our members.

Replacement and reduction of live sentinel animals and refinement of hygiene monitoring of rodent colonies via exhaust air dust analysis

The hygiene status of rodent colonies must be assured to ensure research results are reliable and reproducible. Traditional hygiene monitoring requires live animals to be monitored by bacteriology, parasitology, serology or PCR (Polymerase Chain Reaction) for the presence of subclinical infections that can modulate research results. A new hygiene monitoring method is available which uses special filter pieces (EAD sentinels) mounted in the exhaust air duct of an IVC (individually ventilated cages) rack to collect dust and debris coming from the individually ventilated cages. After sufficient exposure, the filters are sent for PCR analysis of a predefined pathogen panel. Results indicated this non-animal method was just as sensitive at detecting potential pathogens and therefore could replace up to 60 per cent of the sentinel animals each year when implemented in a new hybrid hygiene monitoring programme using EAD technique in two quarters and the traditional live sentinel method in the other two quarters of the year.

Project name:	Exhaust Air Dust Analysis
Charter article:	2

Reduction of in vivo remyelination experiments by applying AI (artificial intelligence) which enables kinetic analysis of rat primary co-cultures

The research group is interested in finding compounds that increase the remyelination capacity of Schwann cells, which are essential for maintaining the health of peripheral nerves. Primary rat Schwann cells / neuron co-cultures could recapitulate the key features of the myelination and are used to triage compounds for in vivo studies. However, these co-cultures are generally low throughput, variable, and lack the option for kinetic studies. The researchers established a co-culture system with an improved throughput and reproducible results. To replace the immunostaining readout, they also developed the Artificial-Intelligence Deep-Learning (AI-DL) algorithm to predict myelination from bright-field images of live cells. This not only delivers fast and robust readouts, but also enables longitudinal re-myelination kinetic analyses, which provide crucial information for the in vivo study design. With this new approach the number of animals could be reduced by 80 per cent.

Project name:	AI-Enabled Kinetic Analysis
Charter article:	1

7.9 billion

Interpharma members invested CHF 7.9 billion in research and development in 2020.

Organoid culture model from human gut tissue
A member company of Interpharma has developed an innovative organoid culture model which is obtained from human gut tissue. Organoids of this kind, which come from patients, allow important aspects of the human body to be modelled outside a live organism. This system renders animal experiments redundant in several phases of drug discovery and development and allows a more precise extrapolation to humans.

Project name:	Human-Gut-on-a-Chip
Charter article:	1

Soft Agar Colony Forming Assay to replace in vivo tumorigenicity studies for gene and cell therapy products
Gene and cell therapies are a new and promising field. So far, preclinical safety testing is based on a case-by-case approach and fixed guidelines are to be determined. One of the main safety concerns is malignant transformation of the cell material due to genetic manipulation, which could lead to tumour formation in patients. Conventional assays for tumorigenicity assessment are in vivo tumorigenicity studies, i.e. human cells are injected ectopically into immunosuppressed mice and monitored for tumour formation. However, the relevance of in vivo tumorigenicity studies is under dispute: the animal microenvironment does not represent a realistic environment for human cells and not all human tumours are able to engraft in immunocompromised mice. Therefore, in vivo studies could miss crucial safety information. An in vitro alternative for in vivo tumorigenicity studies, Soft Agar Colony Forming Assay (SACF), has been developed. Cells with tumorigenic potential are identified based on their ability to grow anchorage independently, a feature of malignant transformed cells. The SACF has been optimized for the gene and cell therapy products in miniformat and an automated imaging system has been implemented to determine colony count.

Project name:	Soft Agar Colony Forming
Charter article:	1

"The rapid provision of vaccines in the pandemic would not have been possible without animal experiments."

Dr. Thomas Steckler
Associate Director Preclinical Risk Management,
Animal Welfare Strategy Lead, Janssen Pharmaceutica NV

Establishment of a 3Rs scientist role
One member company has established a PhD-trained 3R scientist role to further strengthen a culture of ethical science at the member company and serve as an expert in advancing the reduction, replacement and refinement of animal studies.

Project name:	3Rs scientist role
Charter articles:	1, 3

primART
The well-being of animals that have to be used in research despite the advances in the 3Rs is a focus of Interpharma member companies' efforts. A strong, positive relationship between animal attendants and the animals in their care plays a contributory part in these efforts. This can especially help to reduce stress and foster trust in humans among non-human primates (NHP), which are extremely intelligent and social animals. This relationship can be reinforced by positive daily interactions, e.g. by offering opportunities for activities or play. With this in mind, one member company of Interpharma has introduced a new kind of enrichment for its primate colony that is used for pharmacokinetic studies: the animal attendants offered the animals finger paint and a canvas – and within a few minutes the first primates began to paint on the canvas. While some animals are not interested in the new activity, others have now become real artists, who have their very own style. The primates are actively and voluntarily engaged, and not only are they producing a great many paintings, but the animals and their attendants are also spending a great deal of time together and deepening their relationship.

Project name:	primART
Charter article:	2

In vitro approach for mAbs
The correct characterization of drug candidates for the desired pharmacokinetic (PK) properties is essential for the successful development of biotherapeutic products. A member company of Interpharma has developed a cell-based in vitro approach for predicting the elimination of monoclonal antibodies (mAbs) from the human body. Monoclonal antibodies (mAbs) are antibodies which are formed from identical lymphocytes, have an identical structure and bind to the same antigen. With the use of mAb-based biotherapeutics in humans, the so-called neonatal Fc receptor (FcRn) is critical to elimination from the body and substantially slows down its elimination, so that dwell time in the body can be specifically influenced through the effect on FcRn binding. Usually in vivo studies with rodents and non-human primates are used in order to predict pharmacokinetic properties of therapeutic antibodies in humans. Previous studies using in vitro approaches tended to evaluate only a few biochemical properties of therapeutic antibody candidates, and the predictive power was limited. This novel in vitro approach shows exceptional predictive power directly with regard to human PK parameters and delivers valuable and important results for the assessment of pharmacokinetic properties. This not only serves as an alternative to in vivo studies, but also improves the predictive potential, which simplifies the decision-making process when it comes to lead selection and optimization and allows more candidates to be evaluated, which amounts to greater efficiency.

Project name:	Monoclonal Antibodies
Charter article:	1

Internal awards as a means of promoting the 3Rs
Some member companies of Interpharma regularly acknowledge research with internal national and international 3Rs awards. Researchers from different departments have the opportunity to submit their work and developments and are thereby motivated to further advance the 3Rs. The member companies are agreed that animal welfare is a global concern and that everyone has a responsibility for it. It is all about opening hearts and minds to support for the 3Rs. That this is succeeding is apparent from the annual increases in the number and quality for submission for these awards. These awards serve to reward efforts at reducing, refining and replacing animal experiments and fostering engagement for the protection of laboratory animals.

Project name:	Awards
Charter article:	3

National promotion of the 3Rs by the 3RCC
In 2020 the 3RCC, which is supported by universities, industry, the authorities and Swiss Animal Protection, sponsored five projects to the tune of CHF 1.4 million for the replacement, reduction and refinement of animal experiments. In response to the call for submissions in 2020, the 3RCC received 69 preliminary proposals. Half the projects related to replacement, 30 per cent to refinement and 20 per cent to reduction. More than 50 international experts examined the 15 projects for which full submissions were invited. The 3RCC then selected five scientifically high-calibre projects that promised a major impact on the 3Rs. Two projects lie in the field of neurology and one in the field of cancer, two research areas in which a large number of laboratory animals are used in Switzerland. Four of the five projects are aimed at reducing the use of animals or replacing animal studies altogether. With these projects, approaches are being developed that will lead to more reproducible and more reliable results and greater relevance for humans. In the fifth project, a new method for administering medicines is being developed, thereby improving animal welfare.

Project name:	National promotion of the 3Rs
Charter articles:	1, 3, 9

47,000

people were employed in Switzerland's pharma industry in 2020.

Biomedical Research Awareness Day (BRAD)
One Interpharma member company held its third annual Biomedical Research Awareness Day (BRAD) in 2021. BRAD was launched in 2016 by Americans for Medical Progress (AMP) in the US and takes place every third Thursday in April. This day is an opportunity to inform and raise awareness among the company's employees about the need for and benefits of animal research for the development of new medications and therapies. In the Interpharma member company, BRAD was celebrated globally in October with numerous presentations highlighting the company's Culture of Care for the animals, employees and patients as well as recognizing advancements with their global 3Rs (Reduce, Refine, Replace) awards and animal stories in the development of new therapies. At its site in Switzerland, the event was opened by a presentation from the Zoo Basel to highlight the specific role of a modern zoo. The other presentations informed about the training and the roles of animal caretakers and research technicians as well as the recent accreditation of their animal care and research programme by AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care). All this information is important to share with employees in view of the public vote in February 2022 on the complete ban on animal and human clinical trial studies, as well as the import of drugs developed with the help of animals.

Project name:	BRAD
Charter articles:	1, 3, 9

Working groups and projects

Numerous projects and working groups have already been in existence for many years, promoting national and international cooperation in the field of the 3Rs and benefiting the wellbeing of laboratory animals.

AAALAC International (Association for Assessment and Accreditation of Laboratory Animal Care)
The independent, non-profit organization AAALAC promotes the humane treatment of animals in science with the aid of voluntary evaluation and accreditation programmes. More than a thousand institutions, including pharmaceutical companies, universities and biotech firms in 50 countries have been accredited by the AAALAC. Several sites of Interpharma member companies are also AAALAC-certified. Since 2013, Interpharma has had a seat in the delegation of member organizations and since 2020 also has a seat on the Board of Directors, so it can exert a direct influence on the promotion of independent animal welfare certification programmes. To ensure that the monitoring and performance of research with animals and their care is in line with tried and tested procedures, the AAALAC has more than 360 ad hoc consultants, who accompany committee members during on-site visits and make recommendations. These consultants – who also come from Interpharma member companies – can offer expertise that extends beyond the field of conventional laboratory animal species and in some cases provide additional expertise in fields such as applied neuroscience, behavioural science, toxicology, pharmacology or physiology.

Project name:	AAALAC International
Charter articles:	2, 7
Link:	www.aaalac.org

IQ Consortium (International Consortium for Innovation and Quality)
Member companies of Interpharma are engaged in the IQ Consortium and participate in the 3Rs Leadership Group of this consortium. The group was established to promote the exchange and realization of high-quality scientific practices and thus to advance the principles of the 3Rs in animal research aimed at the discovery and development of new medicines, vaccines, medical devices and health products for use in humans and animals. The subgroup European Liaison Working Group, with which Interpharma maintains official contacts, promotes the exchange of 3Rs expertise and their mutual interest in similar objectives being pursued both in the US and in Europe. In addition to a global 3Rs award programme, the group also offers 3Rs training and continuing education courses.

Project name:	IQ Consortium
Charter articles:	1, 3, 9
Link:	www.iqconsortium.org

Interpharma Animal Welfare Working Group
The Animal Welfare Working Group is one of the seven permanent working groups of Interpharma. Various company representatives and also a representative of the University of Zurich meet regularly to address the ongoing improvement of animal welfare and the promotion of the 3Rs. In keeping with the 10-point charter, which was launched in 2010, this group commits to produce an annual report on its activities and advances in the area of the 3Rs and animal welfare.

Project name:	Interpharma Animal Welfare Working Group
Charter articles:	1–10

Building 098: an ultramodern research facility
In its effort to bolster the 3Rs, Roche is developing alternative methods and approaches to replace animal experiments. These include, for example, the use of animal and human cell cultures, computer simulation or individual organs-on-a-chip (organs replicated on a microscopically small scale with human or animal cells). These make preclinical studies more precise and more informative and allow the number of animal studies to be reduced. But animal experiments can still not be eliminated altogether – and this for a number of reasons, including the fact that they are required by law. Roche has therefore built a new, ultramodern research facility, where animals and their welfare are placed centre stage. At the same time, work processes are to be arranged more effectively and efficiently and the quality of the workplace thus enhanced. Each floor can be converted within four weeks, thereby making it easy to adjust to constantly changing requirements. Aside from animal welfare, the protection of employees' health is also a central concern: cages are automatically cleaned and replenished, which reduces allergic reactions among employees. Mobile robots manoeuvre heavy loads, reducing physical stresses and strains on the staff.

The new in vivo research facility is already fully digital, thus allowing many parameters to be gathered online in future. It also offers an ultramodern and attractive environment both for animals and humans in order to achieve the best possible results from in vivo research and further advance the vision of the 3Rs to Replace, Reduce and Refine.

Project name:	Building 098
Charter article:	1

EPAA (European Partnership for Alternative Approaches to Animal Testing)
The EPAA platform, a voluntary partnership between the European Commission and various industrial sectors that builds on the exchange of know-how and resources to improve the development, validation and acceptance of animal-free methods of research, is actively supported by Interpharma members. In the past two decades, the EPAA has organized around 50 workshops and released numerous publications. The EU Commission and 37 companies from seven industrial sectors (chemicals, pharmaceuticals, cosmetics, perfume, soap and detergent industries, as well as animal health) agreed in 2016 to a further five-year collaboration up to 2020. The focus is on cooperation with international supervisory bodies and national regulatory agencies. The EPAA aims to continue its intensive support for the international harmonization of regulatory safety requirements, whenever appropriate and possible.

Project name:	EPAA
Charter articles:	1, 2, 8
Link:	ec.europa.eu/growth/sectors/chemicals/epaa

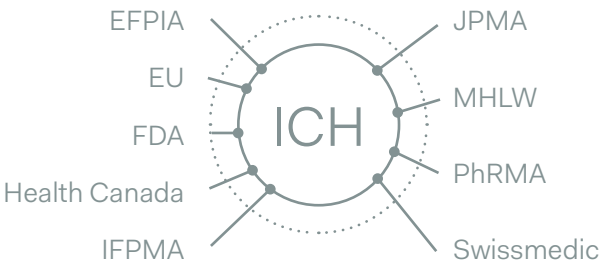
"Medicine has significantly benefited from groundbreaking discoveries in basic biological research and their implementation through applied research. Animal experiments provide an essential pillar of support in this progress."

Nathalie Stieger
Head of Group Government Affairs, Roche

70%

According to the Health Monitor 2021 from gfs.bern, 70 per cent of Swiss voters are in favour of a redistribution of healthcare investments into the research and development of new medicines and vaccines.

ICH
(The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use)
ICH brings together regulatory authorities from Europe, Japan and the US with the pharmaceutical industry to discuss scientific and technical aspects of pharmaceutical product registration. The purpose of the ICH is to harmonize the tests used during the research and development of new medicines and the technical standards and requirements for product registration. This standardization is intended to ensure a more cost-effective deployment of resources and to eliminate unnecessary delays in the global development and availability of new medicines. The harmonization process is complex and can take several years. It refers to the areas of quality, safety (which is where animal experiments come in), efficacy and multidisciplinary fields.



Project name:	ICH
Charter articles:	1, 8

TEDD (Tissue Engineering – Drug Development)
Organ-like human tissue and cell models are of major importance for drug development and for the assessment of compounds. The National Competence Centre TEDD pools and transfers knowledge and technology to promote the further development and application of in vitro cell and tissue culture. New technologies that offer a physiologically more relevant representation of the function and structure of healthy and diseased tissues and organs are gaining ground. However, they are still in an early phase of development and are only of limited suitability for routine use. To exploit their full potential, there is a need for new methods of analysis to be developed, along with the further development of controlled and standardized production of tissues, preservation, automation, routine application and quality control. Concrete research projects in a network of partners from various stakeholders – including several member companies of Interpharma – have resulted in a platform that is actively helping to shape the development and application of alternative test methods for routine use in industry.

Project name:	TEDD
Charter articles:	1, 8

Research for Life association
The independent association Forschung für Leben (Research for Life) was founded with the aim of informing the Swiss population about the importance and latest results of biomedical research. The idea is to foster dialogue between scientists and the lay public and to explain in clear and straightforward language not only the benefits but also the hazards of research. Besides the regular publication of the brochure “BioFokus” and the awards it grants to high school graduates for end-of-school projects, the association also makes a so-called gene laboratory available to any schools that are interested. Interpharma has supported the association financially for several years and cooperates with it especially in the field of animal welfare and animal protection.

Project name:	Forschung für Leben
Charter articles:	1, 3, 9
Link:	www.forschung-leben.ch

–2.8%

In Switzerland, 2.8per cent fewer animals were used for research in 2020 than in 2019.

3Rs Competence Centre (3RCC)
The national 3Rs Competence Centre (3RCC) was founded on 27 March 2018 to promote the principles of the 3Rs in Switzerland. Along with 11 universities, participants in the 3RCC include Interpharma, Swiss Animal Protection and the Federal food Safety and Veterinary Office (FSVO). Its objectives are to sponsor high-quality 3Rs research projects, to develop a strategy for 3Rs-based training and continuing education, and to establish a professional communications strategy. The 3RCC provides access to the latest information concerning the 3Rs and alternatives to animal experiments for all actors involved. The centre offers its services to authorities, teaching and educational institutions and other interested groups. It also monitors the progress achieved in these areas in Switzerland. Before the establishment of the national centre, 3Rs research projects were supported and sponsored for 30 years by the 3Rs Research Foundation Switzerland. In 2021, the Swiss government launched the "National Research Programme NRP 79 Advancing 3Rs – Animals, Research and Society" aimed at accelerating the development of 3Rs applications with funds amounting to CHF 20 million up to 2028. The 3Rs Research Foundation, which preceded the 3RCC from 1987 to 2018, financed 3Rs research projects to the tune of around CHF 20 million.

Project name:	3RCC
Charter articles:	1, 3, 9
Link:	www.swiss3rcc.org

EFPIA network for animal welfare
Member companies of Interpharma contribute ideas for high animal welfare standards on a pan-European level in the EFPIA Research and Animal Welfare (RAW) Group. One of the primary functions of this group is to collaborate actively in efforts to effectuate the EU Animal Welfare Directive 2010/63 in EU Member States. The implementation of this directive was reviewed in 2017 by the European Commission and found to provide a solid foundation for regulating the protection of animals used for scientific purposes. The group also advocates for an open exchange of ideas and good collaboration with other organizations that support research in the area of the 3Rs. The group is made up of experts in toxicology, pharmacology, ethics, law, public affairs and animal welfare, as well as observers from academic and regulatory institutions. In addition, the EFPIA publishes an annual 3Rs report online.

Project name:	EFPIA network for animal welfare
Charter articles:	1, 2, 8, 9

Animal Research Tomorrow
The goal of Animal Research Tomorrow (formerly the Basel Declaration Society) is to reinforce public trust in animal-based biomedical research and to foster open and transparent communication between researchers and the general public. It seeks to help ensure that ethical principles such as the 3Rs are applied in animal research worldwide. At present, more than 4500 researchers around the world have signed the declaration. The activities of Animal Research Tomorrow include participation in meetings and events concerning animal experiments, regular publication of the magazine "Mice Times" and also the hosting of an international congress every two years. In addition, the organization awards an annual prize for the harmonization of quality standards in the handling of laboratory animals. Interpharma and its member companies have supported the project of Animal Research Tomorrow financially for years.

Project name:	Animal Research Tomorrow
Charter articles:	1, 9
Link:	animalresearchtomorrow.org

Internal training
Every year, a member company in Switzerland offers an array of federally approved training courses and one special day of continued education, enabling associates that work with animals in research to meet their statutory training requirements.

Topics of the training day include:
- The science behind and impact of award-winning 3R projects
- Prevention of heat loss in mice during anaesthesia
- Introduction to a gentle handling procedure for mice (tunnel handling)
- The use of programmable pumps in oncology research for compound delivery to refine and reduce animal engagement
- Update on the statutory initiatives in Switzerland that impact animal research
- On the training day, information on any changes, including legislation and directives, are also provided. This ensures that the employees are informed about the current state of the legislation as well as on the concerns of the Animal Experimentation Commission.

Furthermore, practical training is also offered in this member company via the Training Services group. Training is provided to all new employees in the field of animal research in order to ensure uniform standards. Additionally, special events and advanced training are also offered for experienced employees. These continued education courses can be officially recognized as counting toward the required continued education days.

Project name:	Internal training
Charter articles:	1, 3, 9

The Animal Welfare Charter of the pharmaceutical industry established milestones that were also recognized by academic researchers to be a groundbreaking development.

Joint audits of Interpharma member companies
Research institutions as well as their partner and subsidiary companies which conduct animal experiments on behalf of Interpharma members commit to comply with technical requirements and ethical standards in the husbandry and care of laboratory animals. Some member companies of Interpharma regularly carry out joint audits at external research partners and breeders all over the world after prior notification. These audits not only serve to ensure that standards are harmonized and laboratory animals protected, but also help to develop expertise. The sharing of this information provides for optimum implementation of the legal requirements and also simplifies further-reaching efforts to apply the 3Rs. The audit results are jointly discussed and treated in confidence within the member companies. The decision on whether to enter into a business relationship with the audited organization is the responsibility of the individual company. Besides the jointly conducted audits, member companies check the compliance in their own research institutions worldwide with the defined quality standards in individual procedures. All the criteria checked are recorded in writing and have global validity.

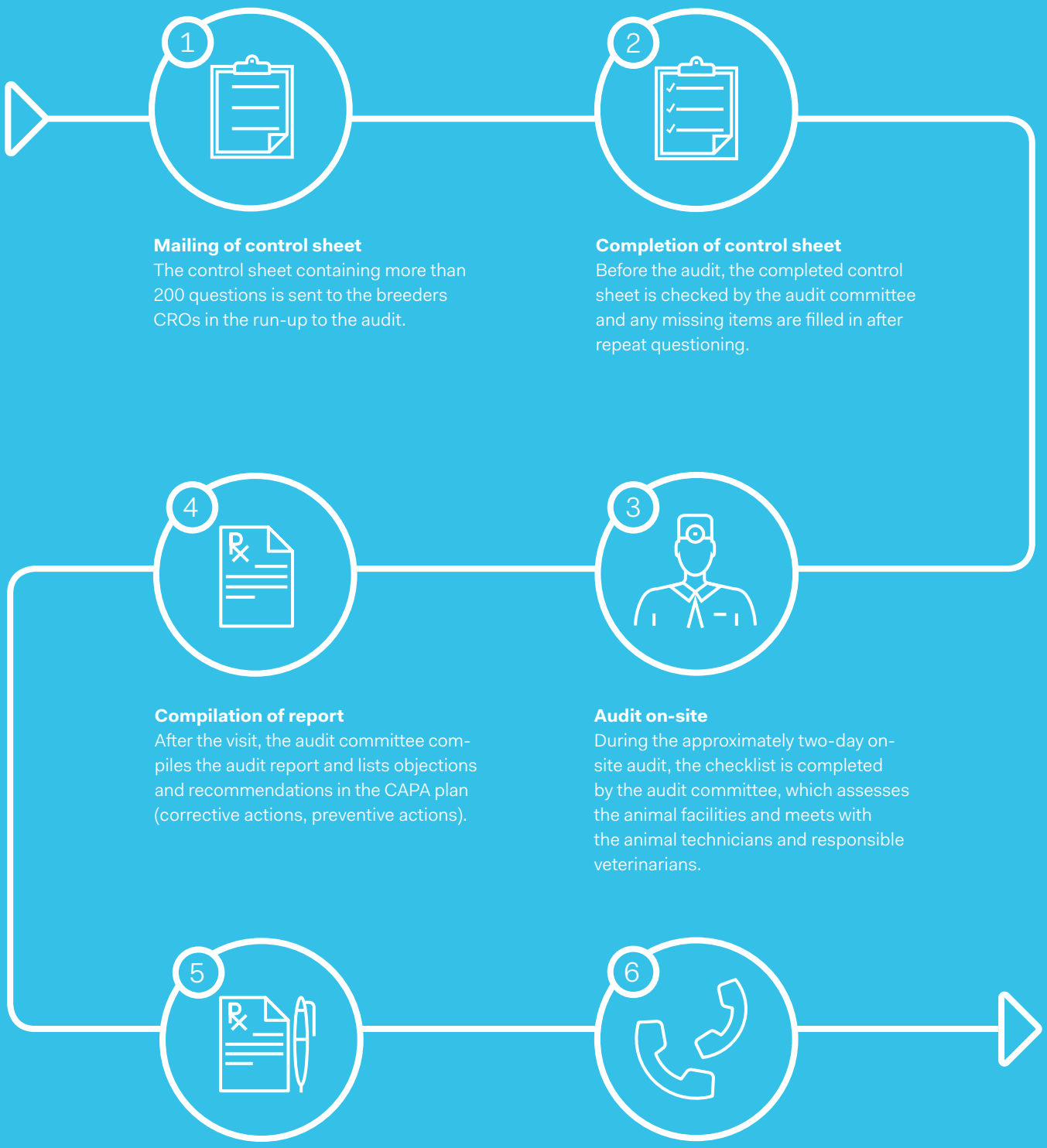
Project name:	Interpharma audits
Charter articles:	4–6

Dialogue with Swiss Animal Protection
Interpharma has been in dialogue with STS (Swiss Animal Protection or SAP) for more than eight years. Some years ago, the two organizations viva3R and the Zurich animal protection group Zürcher Tierschutz also joined the dialogue. Their meetings, which take place twice a year, serve to foster mutual understanding, to elucidate questions of animal welfare and to address technical questions on animal experiments and the protection of laboratory animals.

Project name:	Dialogue with STS
Charter article:	9

The audit process

Some member companies of Interpharma have been conducting regular joint audits at breeders and external contract research organizations (CROs) worldwide since 2014.



Mailing of control sheet
The control sheet containing more than 200 questions is sent to the breeders CROs in the run-up to the audit.

Completion of control sheet
Before the audit, the completed control sheet is checked by the audit committee and any missing items are filled in after repeat questioning.

Compilation of report
After the visit, the audit committee compiles the audit report and lists objections and recommendations in the CAPA plan (corrective actions, preventive actions).

Audit on-site
During the approximately two-day on-site audit, the checklist is completed by the audit committee, which assesses the animal facilities and meets with the animal technicians and responsible veterinarians.

Finalization of report
The breeder/CRO then has the opportunity to respond to the report and make possible amendments.

Final discussion
In a final conference call, any unresolved questions are clarified and final actions defined – timeframe, definition of contact person and possible repeat visit.

Alternatives to Animal Experimentation – ALTEX
www.altex.ch

American Association for Laboratory Animal Science – AALAS
www.aalas.org

Animalfree Research
www.animalfree-research.org

Association for Assessment and Accreditation of Laboratory Animal Care International – AAALAC
www.aaalac.org

Basel Declaration
www.basel-declaration.org

Competence Centre TEDD
www.zhaw.ch/de/lsfm/forschung/chemie-und-biotechnologie/competence-centre-tedd

European Federation of Pharmaceutical Industries and Associations – EFPIA
www.efpia.eu

European Partnership for Alternative Approaches to Animal Testing – EPAA
www.ec.europa.eu/growth/sectors/chemicals/epaa

Federation of European Laboratory Animal Science Associations
www.felasa.eu

Institute for Laboratory Animal Research
www.dels.nas.edu/ilar

International Consortium for Innovation and Quality – IQ
www.iqconsortium.org

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use – ICH
www.ich.org

International Council for Laboratory Animal Science
www.iclas.org

Johns Hopkins University Center for Alternatives to Animal Testing – CAAT
https://caat.jhsph.edu

National Centre for the Replacement, Refinement & Reduction of Animals in Research
www.nc3rs.org.uk

New Jersey Association for Biomedical Research
www.njabr.com

Schweizerische Gesellschaft für Versuchstierkunde – SGV
www.naturwissenschaften.ch/organisations/sgv

Schweizer Tierschutz – STS
www.tierschutz.com

Swiss 3Rs Competence Centre – 3RCC
www.swiss3rcc.org

Themenportal Tierversuche
www.naturwissenschaften.ch/topics/animal_experimentation

Tierversuche verstehen – eine Informationsinitiative der Wissenschaft
www.tierversuche-verstehen.de

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Impressum
11th Annual Report, published in 2021 by:

Interpharma
Association of research-based pharmaceutical companies
in Switzerland
Petersgraben 35
Postfach
4009 Basel
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Editorial office:
Interpharma

Supported by:
Members of Interpharma, 3RCC

Realization:
Sensor Advice GmbH
www.sensoradvice.ch

Disponible en traduction française
Erhältlich in deutscher Sprache

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About Interpharma

Interpharma was founded in 1933 and is the association of research-based pharmaceutical companies in Switzerland. Overall, the 23 member companies account for more than 90 per cent of the market share for patented medicines in Switzerland and invest CHF 7.9 billion in research and development in Switzerland each year. Interpharma is a driving force for an efficient and high-quality healthcare system that offers patients early access to innovative therapies and the best-possible care. Both at home and abroad we campaign to ensure that patients get first-class healthcare, innovations are rewarded and our industry is able to make a substantial contribution to prosperity, growth and competitiveness in Switzerland.

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