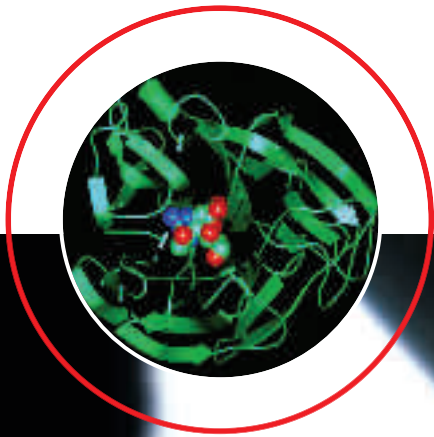
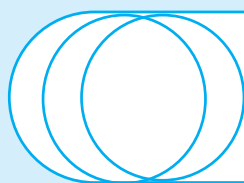


Animal research and human medicine



A resource for schools



Contents

Introduction	1
Why we need medicines	2
Bringing medicines to patients	4
Following up an idea	5
Research and testing	6
Epilepsy – the quest for control	9
Using animals in research	10
Developing alternatives	12
The law, compassion & respect	14
What the law says	15
Penicillin – the wonder drug	16
Cystic fibrosis	18
Glossary (see words in bold)	19
Food for thought	20

This booklet is designed to support teachers working with pupils on the issues surrounding the use of animals in medicines research. Whether used in the context of Citizenship, PSE, Science, English or RE, it aims to provide a useful resource for both teachers and pupils across the UK.

The ABPI wishes to thank the Science Photo Library, Wellcome Photo Library, the University of Newcastle upon Tyne, Corbis, the Institute of Animal Technology and GlaxoSmithKline.

This booklet was produced by the
**Animals in Medicines Research
Information Centre**

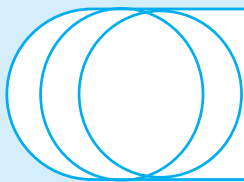
part of
**The Association of the British
Pharmaceutical Industry**



Medicines for a healthy future

12 Whitehall
London SW1A 2DY
Tel: 0870 890 4333
Fax: 020 7747 1411
www.abpi.org.uk

Teachers' Notes and Pupil Worksheets for
"Animal Research and Human Medicine" can be found on our
website www.abpi.org.uk/amric/amricpublications.asp



Introduction

People have always used animals for food, warm clothing, transport and all kinds of work, such as pulling ploughs and carrying loads. How do we feel about the other ways in which they are used? Is it acceptable to eat meat? What about wearing leather and wool? Should we have new medicines if this involves using animals in research? The ‘rights’ and ‘wrongs’ of such use of animals have been debated for hundreds of years – and the

Today, most of us are concerned about the protection of our natural world and have respect for the needs of other creatures as well as human beings. At the same time, our rapidly growing knowledge of science and technology presents us with increasingly complicated moral issues. To try to make sure that science is used in an **ethical** way, society needs to discuss these issues. Unfortunately, sometimes there are no easy answers and difficult choices have to be made.

This book looks at the use of animals by people who carry out research into new and better medicines. All new medicines are studied in animals before researchers are permitted to test and use them in people.

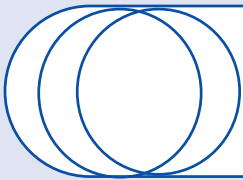
Many people accept the use of animals in this way because of the benefits to human health and well-being it helps to bring about, but some of us may feel that animal research is simply wrong, whatever its importance to medical progress.

Some feel that the morality of using animals depends on the aims and achievements of the experiments, whether the animals are treated **humanely**, or on the seriousness of the illness involved – maybe they can accept the use of animals in trying to develop a cure for cancer but not for migraine, even though these headaches can be very painful and, for some unlucky people, occur frequently.



Medicines successfully prevent or treat many common diseases, helping millions of people to live longer and have a good quality of life.

The use of animals in medical research is an issue on which there are many differing views, and opinions can change with knowledge and experience. In order to make up your own mind it is important to understand all aspects of the debate. This booklet sets out to explore the discovery, development and safety testing of new medicines – using real case studies as examples and presenting the current laws relating to animal experiments. We hope



Why we need medicines



Having a healthy lifestyle gives us a better chance of staying fit and well.



When SARS (Severe Acute Respiratory Syndrome) was first diagnosed, scientists worked fast to identify the virus which causes the disease and find out how it spread. The problem was controlled fairly quickly although not before nearly 800 people had died.

The state of our health is important to us – most people want to be as healthy as possible.

That's why 'How are you?' is the most common greeting in many languages!

Being ill can be very unpleasant, limit what we are able to do and even shorten our lives. And illness affects the whole of society, not just individuals and the people who care for them, because our absence from school, work and family

What causes illness?

Infectious illnesses like colds and tonsillitis are caused when **micro-organisms** such as bacteria and viruses invade our bodies. Other diseases like cystic fibrosis are the result of the genes we inherit from our parents and grandparents. Many diseases are the result of a combination of bad luck and genetics.

Our lifestyle also affects our well-being. Eating a balanced diet, not smoking, drinking alcohol only in moderation, taking plenty of exercise and getting enough rest all help to protect our health. But lifestyle factors alone may not prevent us getting ill, nor cause disease. Some people with unhealthy habits stay well (though they are unlikely to be full of vitality). But your lifestyle can seriously tip the balance one way or the other.

What's more, even after recovery, disease can sometimes have knock-on effects on overall health. Measles, for instance, could leave children with a legacy of blindness or brain damage, while some teenage boys and men are left infertile by mumps.

Dealing with new disease

Many of the diseases that affect us have been around for thousands of years, but new diseases still appear. AIDS and SARS are just two reminders that we need to be constantly on our guard against new infections. We need to know what causes new diseases, how they are spread and what health education programmes, medicines and vaccines might help to control them.

Preventing illness

Persuading people to make healthy lifestyle choices means they are less likely to develop heart disease and some cancers. Even more importantly, good hygiene, proper sewage disposal and clean drinking water are vital in preventing disease. Prevention can also involve the use of medicines. Vaccinations have almost eliminated killer diseases like diphtheria and polio and have wiped out smallpox worldwide. And preventing one disease can remove the risk of other, linked health problems that can arise later.

The more we know about a disease, the easier it is to prevent or treat.

Treatment or cure

There are many different types of medicines available to us today, some of which treat and cure diseases, while others simply make us feel better and therefore able to get on with our lives. They include:

- Medicines that destroy infectious organisms – e.g. **antibiotics**
- Medicines that destroy cancer cells – e.g. **cytotoxins**
- Medicines that replace missing chemicals in the body – e.g. **insulin**
- Medicines that relieve inflammation or pain – e.g. **ibuprofen, morphine**

Improving Medicines

Many of the medicines we already have work well – but there is still a need for them to be improved. Medicines work better for some people than for others and some people will experience side effects when others don't. For example, there are several powerful and effective medicines used to help people with epilepsy live active lives. But for some people, the medicines simply don't work well enough – so more new epilepsy medicines are badly needed. Scientists and doctors are constantly trying to improve existing medicines as well as discover new ones.



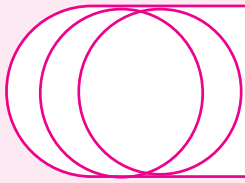
Modern medicines have made it possible for almost everyone with asthma to lead active lives.

Tackling asthma

Asthma is becoming increasingly common. About one in eight children is affected, although many outgrow the problem later. It often runs in families. Asthma causes bouts of wheezing, breathlessness, coughing and tightness of the chest.

Asthma usually starts with mild allergies which often pass completely unnoticed. The most common allergies are to house dust mites, cat and dog fur and pollen. For some people, regularly breathing in these **allergens** irritates the cells that line the airways to the lungs, so they are always slightly inflamed and over-sensitive. These over-sensitive airways then react to triggers like cold air or exercise to cause an asthma attack. The airways swell up and narrow, so breathing becomes difficult, which can be very frightening.

In the past, most people with asthma did no exercise, to avoid making their airways work too hard. Today, most people with asthma learn how to manage their illness so they can lead active lives. This is done largely by gaining a good understanding of their condition and the proper use of two different types of asthma medicines. Some of the medicines are used regularly to keep the background inflammation of the airways under control. This makes asthma attacks much less likely to occur. Other medicines are used at the first signs of a problem, to open up the airways and make breathing easier. Today, we have Olympic athletes with asthma, something that would have been unthinkable in the past.



Bringing medicines to patients

“The NHS would be unable to function effectively were it not for the availability of medicines and treatments that have been developed or validated through research using animals”

Department of Health

All of us take medicines at some time, for example, childhood vaccinations, medicines to control long-term conditions like asthma and epilepsy or antibiotics to clear up a bacterial infection. We are so used to having these benefits that we take them for granted. But every medicine is the end result of a long, expensive process to discover or identify a potentially useful compound and then develop it to be as safe and effective as possible. Only a tiny number of compounds make it through this long process.

New medicines – what really matters

The starting point for developing new medicines is an understanding of how the human body works and how it is affected by a particular disease. A useful medicine may treat many thousands or even millions of patients. For any medicine to be allowed to be prescribed, an enormous amount of information must be collected to demonstrate that it is:

- **Effective** – it must prevent or cure the illness, or relieve the symptoms for the patient. For instance, a compound might seem to be useful in the early stages of research but it must also be able to be absorbed into the body. It won't help the patient if it can't reach its target or it is destroyed by the body before it has a chance to work.
- **Safe** – it has to deal with the problem without causing unacceptable side effects, taking into account the seriousness of the illness the medicine is designed to treat. For instance, will it affect blood pressure or maybe collect in the bone (storing up trouble for the future), rather than being passed out of the body once it has done its work?
- **High Quality** – the medicine must be able to be manufactured to a high standard every time and it needs to remain stable so it can be stored without deteriorating for a given period of time.

Research into a new medicine has to make sure that all these conditions are met. This is why it takes a very long time – up to 12 years and around £500 million – to bring a new medicine into the doctor's surgery.

When people consider medicines research, they may also think about the use of animals in testing. Animal testing is a small but crucial part of the research process for all new prescription medicines.

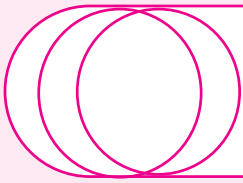
INFORMATION FROM ANIMAL TESTS ARE REQUIRED BY LAW

In the UK, the law known as the Animals (Scientific Procedures) Act 1986 (explained later in this booklet), controls the use of animals in research.

At the same time governments around the world have to do their best to see that new treatments can be used safely. As a result, there are laws that demand animals are used in medicines testing. Below is a quote from the European legislation about the testing of new medicines. The UK must abide by these rules.

“Clinical trials must always be preceded by adequate **pharmacological** and **toxicological** tests, carried out on animals in accordance with the requirements.....”

(This is from European Directive 2001/83/EC, Annex 1 Part 4)



Following up an idea

In the 1920s an American veterinary surgeon was called out to a number of cases of uncontrolled bleeding (haemorrhage) in some cattle. At first he was puzzled as to the cause, but eventually began to think that the outbreak might be connected to some spoiled clover which the cows had eaten. The food had been stored and had begun to go bad, so perhaps a natural chemical in the fresh clover had changed, becoming harmful in the spoiled

To test his theory, the vet designed the following experiment: he fed spoiled clover stalks to one rabbit and fresh stalks to a second rabbit, the control. The first rabbit haemorrhaged and died, but the second thrived, confirming his idea that something in the spoiled clover caused the bleeding. Obviously, the cattle would not be given the clover again but, even more importantly, the vet's observation was to have a major impact on medicine.

The story of the haemorrhaging cows attracted lots of interest, because scientists wondered if the substance in the plant that caused bleeding in cattle and rabbits might also prevent blood clotting in people.

Blood clotting is essential, as it seals a wound. However, it is dangerous if the blood clots too much. A clot in an artery can block the circulation of blood, causing a heart attack or **stroke**. If something in the clover could prevent clotting, the scientists thought that it might be used (in a safe concentration) to prevent blood clots.

To test this **hypothesis**, scientists had to find out which of the many naturally occurring chemicals in the clover was causing the bleeding, and identify its properties. In 1939, using a test developed with specially bred rabbits, the chemical was discovered to be a form of coumarin. When they tested the compound they found it did indeed prevent blood clotting.

Further research with animals was needed to find out how coumarin caused the bleeding and as a result of the research a range of medicines called **anti-coagulants** – based on coumarin – was developed. Both the vet and the scientists followed an experimental process which is the basis for all investigative work in science.



Although the original problem was observed in cattle, the research which followed used rabbits which are much smaller and easier to manage.

THE EXPERIMENTAL PROCESS

OBSERVATION

HYPOTHESIS (POSSIBLE EXPLANATION)

- What do you think should happen if your idea is correct?
- What information (data) will you look for and how will you collect it?
- What will you vary and what will you keep the same?

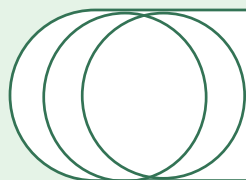
EXPERIMENT

ANALYSING THE RESULTS

- Do they support your hypothesis?
If so –

FURTHER EXPERIMENTS

- To refine your ideas



Research and testing

The role of computers

When scientists understand a disease process and the structure of a molecule that might help, they can use computers to design new molecules that may help deal with the problem. Sometimes they find active chemicals in plants and other living organisms and then computers can design similar compounds that can do the same job.

Computers are also used alongside high-tech robotic **in vitro** systems to check rapidly through tens of thousands of known compounds at enormous speed to pick out ones with a useful characteristic. That doesn't mean those compounds will work in the body, but it is a good start.

Animal research and testing

When body systems work together, they create new conditions which do not exist in tissue cultures. For example, the digestive system may destroy a medicine before it reaches its target, the potential medicine may be converted into something entirely different which is useless or harmful. It may be passed out of the body before it has time to work, or the medicine may affect other systems, indirectly causing problems like raised blood pressure or organ damage. Animal testing enables scientists to identify most of these problems before a medicine is given to people.

The first stages of animal studies are used to show that a medicine is likely to have the desired effect. If a compound looks promising in animals, then more extensive safety testing will be carried out. Potential medicines that seem to have a reasonable chance of being effective and safe from animal tests will then be tested in small groups of human volunteers, while further animal testing continues at the same time to look at the effects when a medicine has to be taken for a long time.

Animal testing is required by law. See page 5

In vitro screening

Specialised cells, tissues and simple organisms like yeast can be grown in the laboratory. Potential new medicines are tested using these systems. These tests give scientists a valuable guide to compounds which might be useful as medicines. Big advances in the methods for growing cells in culture and keeping them alive have made this type of research increasingly valuable. However, the conditions in a laboratory culture, isolated from the influences of other organs and cells, are very different from those in the body, so it would not be safe or ethical to take compounds straight from this stage of testing and give them to people.

Clinical trials (human testing)

Testing in people usually begins in healthy volunteers. They are given very small doses of the new medicine over short periods. The way their bodies react to, or have an effect on, the medicine is monitored and compared with the animal data. Scientists are always aware of possible species differences and check for them as they go along. Also, some side effects can be difficult to see in animals, such as headaches or mood swings. If all goes well, the dose is slowly increased to realistic levels. Doctors must find out how effective the medicine is in the patients it is meant to help and look for any unexpected side effects.

Scientists must get permission from a special government agency, the **MHRA**, to begin tests in people. People are only included in these trials if they agree to take part and the trial itself has been approved by special ethical committees. At first, the number of patients will be small. Later, the studies can broaden until there is enough information to decide if, for what type of patient and in what dosage the medicine should be licensed.



First, ideas are developed and the disease targeted, then:

Search for possible **therapeutic** compounds – this includes computer design of new virtual molecules and screening of many thousands of existing molecules. These have been **synthesised** or found in micro-organisms, animals or plants.

New compounds synthesised in the lab



In vitro screening – testing the potential medicines on cell cultures, tissue cultures and lower organisms, like yeast. Most compounds are rejected at this stage.



Animal research & testing – the small number of molecules that have made it through the first stages are now studied in animals so that researchers can get a better understanding of their possible effectiveness and then their safety both in the short and long term. This gives researchers and doctors the information they need to decide whether, and if so at what dose, the medicine can begin to be tested in people.



Clinical testing on people begins with *human Phase 1* trials on a small number of healthy volunteers, to start investigating the safety of the medicine and consider the best dosage. Data is checked with the results from the animal studies to look for any species differences that might be relevant, before going onto the next stage. *Phase 2 trials* run with a small number of patients who have the target disease. *Phase 3* trials continue this with a larger number of patients

Research into new medicines is made up of three main areas: non-animal research (computer and *in vitro* work), animal research and clinical research in people. The three types of investigations are all needed at different stages of the research. This flow chart gives a simple explanation of the development of a new medicine.

If the medicine has passed all the trials, the company sends all the data to the **MHRA**. If, after rigorous evaluation of the data, the **MHRA** is satisfied with the research, it will recommend the medicine be granted a licence, along with conditions on its use. The medicine will continue to be monitored after it becomes available.

Here you can see some of the particular benefits gained from *in vitro* testing, animal and human testing – and some of the limitations of which human scientists and doctors have to be aware.

IN VITRO TESTS CAN

- Tell whether a new compound has the desired effect on isolated cells or tissues
- Show certain hazards caused by direct effects on the cells
- Suggest the most promising chemical leads to follow

ANIMAL TESTS CAN

- Show what happens to the compound in complete living systems
- Suggest which compounds are likely to be effective in humans
- Help to determine whether a compound can begin to be studied safely in people and at what starting dose

HUMAN TESTS CAN

- Show that a medicine is effective in people and at what dose
- Confirm side effects that were anticipated from the earlier stages but judged to be acceptable
- Identify any potential hazards that were not seen in the earlier research

IN VITRO TESTS CANNOT

- Tell whether the desired effect will occur in a complete living system
- Tell whether the compound will have a harmful effect in a complete living system

ANIMAL TESTS CANNOT

- Predict with absolute certainty what will happen in people

HUMAN TESTS CANNOT

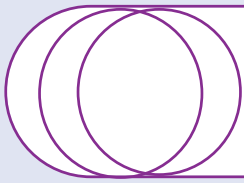
- Prove that a medicine will work for every person who may ultimately take it
- Identify every possible risk for every patient who may take a medicine, as people's genetic make-up and medical histories vary

The stakes are high



Thalidomide is a medicine which was developed in the 1950s, before there were agreed standards for studying the effects of new medicines. The specific animal tests which we now know to be essential were not carried out. Because thalidomide seemed very safe for adults, it was assumed that it was also safe for unborn children and it was given to pregnant women to help relieve the symptoms of morning sickness. This assumption was wrong, and many babies were born with malformations as a result.

The thalidomide tragedy led to a new law which set standards for the testing of all new medicines. Since the Medicines Act 1968, all new medicines must be tested in animals for their potential to harm an unborn child.



Epilepsy – the quest for control

Epilepsy

Epilepsy affects about 1 person in every 200 in Britain, and most are treated with medicines which prevent the unpredictable seizures and allow people with epilepsy to fulfil their potential. Without this control people can hurt themselves as they fall during a seizure (commonly known as a fit), while problems at the top of a flight of stairs or when driving can have serious consequences.

But for some people with epilepsy, the medicines don't work well enough, so their lives are restricted. For others, the side effects of the medicines which control the seizures are fairly severe, so people who could benefit from them don't always want the treatments. More than 60,000 people in Britain affected by epilepsy still have no effective control.

Much of our knowledge of epilepsy comes from studying animals. Rats and mice suffer from seizures which seem very similar to human epilepsy, so they are very useful for investigating medicines to control the seizures. Some breeds of dogs show inherited epilepsy just like people, and they too have been studied to develop medicines which will not only help people with epilepsy but will also treat epileptic dogs.

People affected usually need lifelong treatment, so new and better medicines that work for everyone, are safe to take and have fewer side effects are needed. Animal research plays a vital part in the search for those medicines.



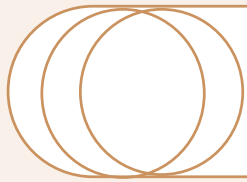
In epilepsy, seizures result from a great discharge of electrical activity in the brain. Symptoms range from brief moments of unconsciousness (petit mal) to the loss of consciousness and rigidity followed by convulsive movements (grand mal). But with good treatment, most people with epilepsy can lead full active lives.

Animal research and the side effects of medicines

There are enormous biological similarities between humans and other animals. The differences are minor compared to the similarities. As a result, most of the effects of medicines in people can be predicted from well-designed animal tests. That is why it would be unsafe and illegal to go straight from computers and cell culture to people.

Even so, animals do not provide complete answers and every researcher knows this. All new prescription medicines also have to go through extensive human testing.

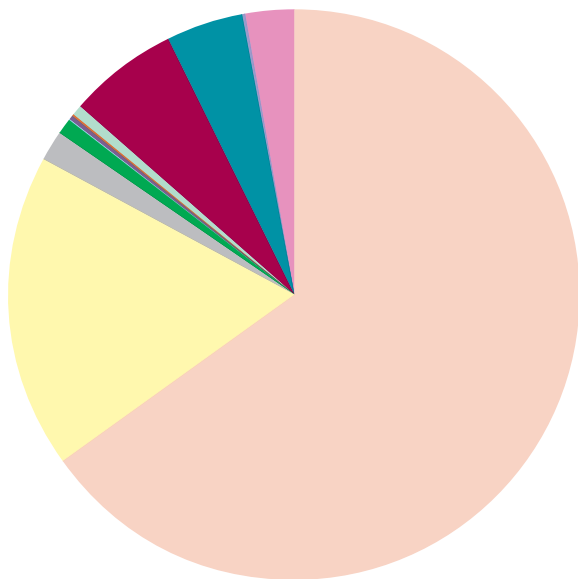
Even after years of human testing, unexpected effects may occasionally be found. There is no combination of research methods that can absolutely guarantee how everyone will react to a medicine. This needs to be weighed against the huge benefits medicines have given us.



Using animals in research

In an ideal world, no animals would be used in medicines research, but at the moment animals have to be used if we want to develop new medicines to help us tackle more diseases successfully. Only a small proportion of all the research carried out to develop a new medicine involves using animals, but that proportion is vitally important for scientists to find out how potential new treatments work in a living organism, before they are tested and used in people. So what are the facts about the animals used in medical research?

Scientific procedures involving animals



Mouse	65.08%	Other carnivore	0.09%
Rat	17.78%	Reptile/amphibian	0.59%
Other rodents	1.72%	Fish	6.23%
Rabbit	0.91%	Bird	4.36%
Cat	0.04%	Primate	0.17%
Dog	0.25%	Other mammals	2.77%

Total approx. 2.79 million procedures in 2003.

(The most recent figures available at time of going to print).

5% of the procedures were non-medical safety testing.

When are animals used?

The use of animals in medicines research is very closely controlled by law through the Animals (Scientific Procedures) Act 1986. It is only allowed if the potential benefits of the research are judged to be important enough to justify the use of animals, and if the research cannot be done in any other way (see p14).

Which animals are used in research?

From the outside, rodents like rats and mice may seem very different to us but, as our DNA clearly shows, the biological differences between us are very small indeed. Most of the effects of medicines in people can be seen in well-designed animal tests, most of which can be carried out on rodents, so these are the animals which are most commonly used in research. Rodents also have the advantages that they are relatively small and easy to keep healthy in well-designed laboratories. And as their natural lifespan is short, information on their long-term health can be obtained quickly. Larger animals are used in research too. The law demands that new medicines are tested on two different types of animals, one a non-rodent such as a rabbit, dog or primate. As the figures show, nearly 84% of all research involving animals is done in rodents. About 0.5% involve dogs, cats or primates.

Where do animals come from?

Virtually all animals used for research into new human medicines are specially bred. Any exception to this would be rare and need special permission. It is very important that the scientists know their animals' exact state of health, the conditions they have been kept in, what they've eaten and how they have been cared for all through their lives. Pets are never used – not only would it be illegal and morally wrong but they haven't all been reared in the same way.

How are the animals kept?

Healthy animals are vital for successful research. They are kept in clean, airy surroundings and those that naturally live in groups are also housed in groups where possible. The animals are provided with an interesting environment in their enclosures and cages, unless this would interfere with the research. Specially trained and qualified animal technicians look after the animals and make sure they are fed, watered and healthy every day. A vet is on call 24 hours a day.

How are the animals used?

The majority of procedures carried out using animals are mild, such as injections and blood sampling. For example, after a new medicine is given, blood samples may be taken to see what is happening to the chemical in the body. But some research does cause distress and researchers must explain to the Home Office, in advance of obtaining a licence, how distress will be minimised. At the end of an experiment, most animals are painlessly killed so that scientists can carry out post mortems. They need to find out the effect of new medicines on the body organs, looking for the early signs of problems which could develop later.

Scientists prefer not to use animals in their research, both for humane reasons and because other methods like tissue culture can give results more quickly and cheaply. Animal tests often take months rather than days. They need stocks of specially bred animals looked after to very high standards and this is expensive – the costs of keeping one experimental dog can run into many thousands of pounds.

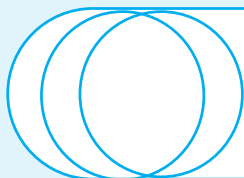
“The BMA believes that animal experimentation is necessary at present to develop a better understanding of diseases and how to treat them, but believes that, when possible, alternative methods should be used.”

The British Medical Association



Social animals like rodents are kept in groups with plenty of opportunity to explore, play and retreat from others if they want to.





Developing alternatives

In recent years scientists in the UK have successfully reduced the number of procedures on animals from 5.5 million in 1972 to under 2.73 million in 2002. Scientists are continually looking for ways to reduce the numbers of animals used in medicines research, and for alternative methods which can give them the information they need to develop safe, effective medicines.



- **Cell and tissue cultures** – These tests are used to the full. In fact, modern pharmaceutical industry research would not be possible without them. These *in vitro* methods allow research in animals to begin at a later stage than used to be possible, saving many animal lives, millions of pounds and months of time. However, cell culture work gives only a very limited picture of what happens in the living body.
- **Computer models** – Scientists can use computers to model how a medicine will work in the body as well as to help them discover and design possible medicines. Essential though they are, computers can only use the information they are given, so the big gaps in our biological knowledge limit what they can help researchers to achieve.
- **Good experimental design** – Scientists around the world are refining existing tests and designing new ones which give more high quality information and need fewer animals.
- **Scientific advances** – Shared scientific expertise and an ever-growing pool of biological knowledge about the human body in health and disease, new technologies such as state of the art scanners which enable us to see what happens inside living bodies, added to the ever improving *in vitro* tests all help to reduce the need for animals. This is at a time when the amount of medicines research being conducted is increasing.
- **Research in other organisms** – Our increasing understanding of biology shows us that we share many genes, body mechanisms and reactions with organisms such as bacteria, yeast, fruit flies and frogs' eggs. This means scientists are able to replace some of the testing done on mammals with work on biochemical pathways in these smaller organisms.
- **Harmonising regulations** – Some animal tests have to be done because they are required by law in another country where the medicine will be sold. Government departments of health along with the pharmaceutical industries in the US, European Union and Japan are working together to agree the tests that pharmaceutical companies have to carry out. These international agreements allow fewer animals to be used in the UK and around the world.

Developing alternatives to animal testing in medicines research is a long and difficult process. At the moment, there is always a point in the medicines research process where we meet barriers to our knowledge that computers and *in vitro* methods cannot yet help us to cross. As our biological, medical and technological knowledge grows, we look forward to a time when animal research may not be necessary. Until then, the priority remains to develop safe and effective medicines involving the considered and compassionate use of animals when necessary.

The '3Rs' are accepted as the basic principles for working towards good laboratory animal welfare and a steady reduction in the need for animal testing

REPLACE

THE USE OF
ANIMALS WHENEVER
POSSIBLE

REDUCE

THE NUMBER OF
ANIMALS NEEDED
TO A MINIMUM

REFINE

TESTS TO CAUSE
ANIMALS THE LEAST
POSSIBLE DISTRESS

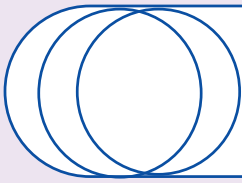
Animals need medicines too

Animals benefit too. Our pets are very important to us. Unfortunately, they are just as likely to get ill as we are, and a sick animal often means a visit to the vet, who has a wide range of medicines with which to treat animal patients. Some of these medicines – such as the vaccines for distemper in dogs or enteritis in cats – were developed specially for animals.

Vets also use many medicines which are exactly the same as, or very similar to, treatments developed for humans. Like human medicines, potential new animal treatments are studied in laboratory animals before they are tested in animal patients. Medicines research in animals doesn't only help people, it helps other animals as well. See if you can find some



examples of animals having similar health problems to people – and needing similar treatment.



The law, compassion and respect

Some people seem to think that scientists can simply decide that they want to use animals in their research and then go ahead. Nothing could be further from the truth. In the UK, research involving the use of laboratory animals is controlled by the most comprehensive legislation in the world. In fact, Britain was the first country ever to pass a law specifically controlling research with laboratory animals – and that was in 1876!



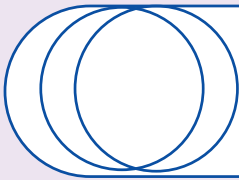
The Animals (Scientific Procedures) Act 1986 balances the needs of research with the welfare of laboratory animals. The use of animals must be kept to a minimum and only the smallest number of animals necessary for the research may be used. Non-animal methods must be used wherever they can realistically supply the required information. The welfare of animals must be protected: any distress an animal is likely to experience must be justified by the potential benefit of the research and kept to a minimum before, during and after experiments.

What is the law for?

Animal tests on human medicines are a legal requirement in almost every country in the world. No new prescription medicine can be developed without the use of animal testing. These laws come under the responsibilities of UK Department of Health and the European Union. However, we have further laws which set out to make sure that animal research is carried out humanely and only when necessary.

The Animals (Scientific Procedures) Act, passed by Parliament in 1986, is overseen by the Home Office. For animal research to be conducted, three separate detailed Home Office licences are required. Scientists and the organisations they work for aim for high standards of animal welfare by ensuring that the research is conducted within a 'culture of care'.

The law also aims to protect animals from unnecessary distress. Most animals experience little or only momentary pain during research procedures – for example, when a blood sample is taken. But some procedures are stressful and researchers must explain, before they start, how they will minimise this. Painkillers or anaesthetics must be used wherever appropriate, although the majority of procedures are too minor to require this – giving anaesthesia would be more troubling to the animals than the procedure itself. If any animal is in severe distress which cannot be relieved, the law states that it must be painlessly killed immediately, whether or not the experiment is complete.



What the law says

The Animals (Scientific Procedures) Act 1986 requires three types of Home Office licences. A laboratory and the research team must obtain all three licences before they can work with animals.

Inspecting laboratories

UK law is clear – animals used in research must be treated with care and respect. A team of Home Office inspectors – all qualified vets or doctors – check up regularly on the laboratories where animal research is carried out. They often arrive unannounced, so no special preparations can be made, and they have to be given free access to the whole area.

Over 3,000 Home Office visits are made each year. Most of these are to check that research involving animals is carried out in a proper, legal and humane way. Most of this type of visit is made unannounced. Other visits are made to give advice, for instance, and make assessments about changes to licences.

“We have a moral obligation to make sure that the animals used in research are healthy and comfortable. But good welfare is also good science, because the way we house and handle animals can affect research results.”

Dr Vicky Robinson

Head of the National Centre for the Replacement, Refinement and Reduction of Animals in Research.

The Certificate of Designation

This authorises the premises where the animals are kept. The Home Office will only grant a certificate to a scientific establishment which is equipped and properly staffed to look after the animals before, during and after the research. The animal houses, laboratories and all the animal care procedures must meet very high standards. Each establishment must appoint someone to be in charge of the day-to-day care of the animals and a veterinary surgeon to advise on their health and welfare. There must be an internal ethical review process to foster high standards.

The Project Licence

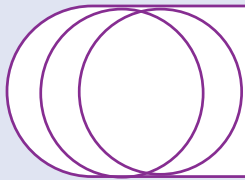
This is granted to the scientist who takes responsibility for the whole research project. Full details of the project must be provided, including:

- The likely benefits of the research
- What non-animal methods are being used and why they cannot be used for everything.
- The procedures that will be used that involve animals
- The likely effects on the animals
- What types of animals and how many animals will be used
- What steps will be taken to minimise any pain or distress the animal may feel

The Home Office considers whether the likely benefits of the research to humans or animals (for veterinary medicine) justify any possible distress to the research animals. If so, a licence is granted.

The Personal Licence

This gives permission to a person to perform certain types of experiments on certain types of animals – and only on approved research projects. It is only given to people who have the necessary education and training. If they decide they need to do extra or different experiments during the research, they have to apply for change to their licence and may have to undergo further training.



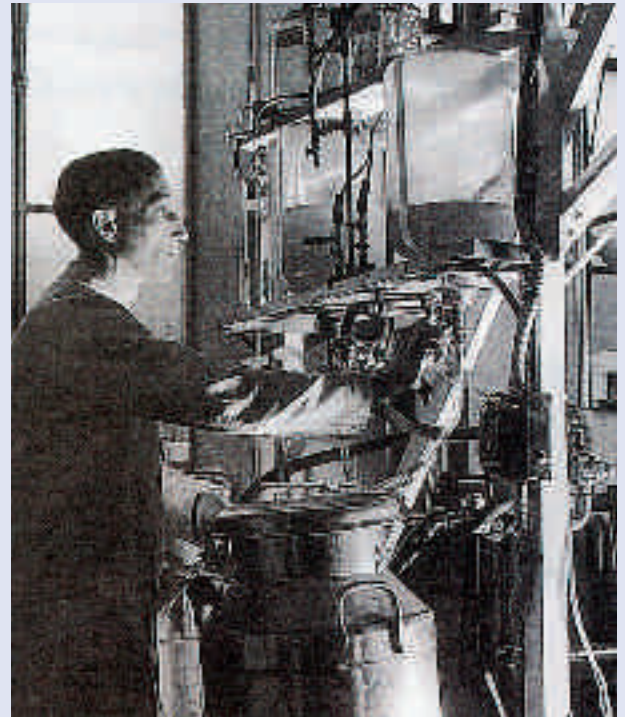
Penicillin – the wonder drug

Before the days of antibiotics, infections lasted longer and were much more serious than today. Illnesses like pneumonia were greatly feared, and even small wounds could be life-threatening if they became infected. Amputation of an injured limb was sometimes the only hope of stopping an infection from spreading through the body. Everyone, even in families with access to the best available health care, could expect to lose family members from bacterial infections that can now be cured.

In 1928, Alexander Fleming made one of the most important observations in medical history while working as a scientist studying bacteria at St Mary's Hospital in London. He returned to his rather cluttered laboratory after a break to find mould growing in a Petri dish containing a bacterial culture. What intrigued him was the fact that bacteria close to the mould had not grown as he would have expected.

The further away from the mould he looked, the more bacteria there were, and he realised that somehow the mould was damaging or killing the bacteria close to it. This chance observation was not just luck, as only a trained and alert mind would have made the connection. If the mould could do this in the Petri dish maybe it would do so in the body!

Original petri dish showing the penicillin at work



Extracting penicillin

To test his idea, Fleming first needed to know how long penicillin would stay active in the body, so he gave it to a number of healthy animals and found that in all of them it disappeared quickly from the blood. This told him that the drug would not have much time to work.

Then, using Petri dishes, he set up experiments to try to understand how the mould harmed the bacteria, but the way the mould seemed to work was so slow that he was convinced it would not work inside the body. He ended the experiment and wrote a paper on this interesting but seemingly disappointing discovery. We now know that Fleming's original hypothesis was correct, but that he came to the wrong conclusion after misinterpreting the results of his Petri dish experiments.

Ten years later Howard Florey, an Oxford professor, and his assistant, Ernst Chain, read Fleming's paper on penicillin during their own search for natural substances to fight bacterial infections. Thankfully, they disagreed with Fleming's conclusion and decided to test penicillin for themselves. The research team carried out a critical experiment.

Eight mice were artificially infected with a lethal dose of bacterium called *streptococcus*. Half of the mice were then given penicillin. At the end of the experiment all four mice treated with penicillin were alive and well, but the four mice that had not been treated were dead. Penicillin worked against bacterial infection in mice!

Soon it was time to try the medicine in human patients, but this was to prove difficult, as the mould was difficult to grow and the result was very impure. And because it disappeared so quickly from the blood, a lot of it was needed. The first patient was a desperately ill policeman who began to make a dramatic recovery when given penicillin. The scientists struggled to produce sufficient quantities of the medicine – even recycling the excreted penicillin from his urine – but unfortunately their efforts were in vain and the man relapsed and died.

In fact, it took a hundred litres of penicillin broth to make enough of the medicine to treat one patient for one day! As the team became more skilled in making the medicine, more patients were treated, but still the numbers were small and it finally took a massive international effort to make penicillin widely available. One breakthrough came when a different strain of penicillin mould was discovered growing on a mouldy melon in America. The new strain was easier to grow and gave a higher yield of the precious penicillin.

Since those early days scientists have continued to search for more antibiotics. They have had a number of successes with chemicals which are often produced by bacteria themselves or by fungi (like penicillin). Doctors now have a range of antibiotics available for treating different types

of infections. These include erythromycin, streptomycin, cephalosporin, tetracycline and – when all else fails – vancomycin.

Most antibiotics work either by interfering with the way bacteria build their cell walls, or by stopping the process of protein synthesis. Human cells don't have cell walls, and the way our cells make proteins is different from the process in bacteria. This means antibiotics can safely interfere in the working of the bacterial cells without damaging the patient at the same time.

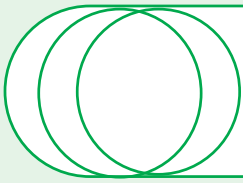
The number of compounds that stay in the body safely AND destroy bacteria are few and far between. And unfortunately, bacteria become resistant to the antibiotics. This is why doctors have to prescribe antibiotics carefully.

Flu, for instance, is caused by a virus, so antibiotics don't work. However, flu can leave a person open to bacterial chest infection. Then, antibiotics may be needed to clear up the infection and avoid the permanent damage infections can sometimes leave behind.

The search goes on for new medicines to help keep bacterial infections at bay.

Fleming in his laboratory





Cystic fibrosis

Cystic fibrosis and gene therapy

Research into human disease progresses slowly in areas where there is no equivalent illness in animals. A good example is cystic fibrosis (CF), a genetic disease which affects about 6,000 people in this country alone. Existing treatments help patients lead longer, healthier lives – average life expectancy has gone up from 25 to 32 in the last 10 years or so – but as Laura's story shows, it's hard work!

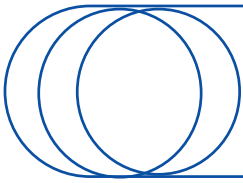
Cystic fibrosis is an inherited disease that affects a number of organs, particularly the lungs, and the digestive system by clogging them with sticky mucus. Until recently, the search for treatments was severely hampered, because scientists were unable to study CF in animals. In 1989 the faulty gene that causes CF in people was discovered, followed by the equivalent gene in mice. By artificially creating the disease in mice, researchers could experiment with new ways in which to override the faulty gene. Scientists have already learnt how to make working copies of the CF gene.

Medicines research is a slow process and they have not yet found an effective way of getting a working gene into the body cells where it is needed but the research continues in cell cultures and in animals. Gene therapy offers us the chance of treating genetic diseases, but to study these human problems means causing genetic disease in animals. We as a society have to decide whether the end justifies the means.

“To control my cystic fibrosis, I take around 30 tablets and an inhaled medicine every day. I also have developed diabetes now, like many people with CF, so I also need two insulin injections a day. Those medicines have all been tested on animals so I'm very grateful to the people and the animals. Without them, I'd be dead.”

Laura Cowell, who was diagnosed with cystic fibrosis when she was 3 months old





Glossary

Allergens – substances which trigger an allergic response in the body e.g. pollen, dust mites

Antibiotics – chemicals which destroy micro-organisms such as bacteria and fungi

Anticoagulants – chemicals which prevent the blood from clotting

Aspirin – a painkiller and anti-inflammatory medicine

Cystic fibrosis – a genetic disease which causes thick, sticky mucus to build up, mainly in the lungs and digestive system

Cytotoxins – substances harmful to cells, (which can be used to kill cancer cells)

DNA – deoxyribonucleic acid, the molecule which carries the genetic information in our cells

Epilepsy – a disorder caused by abnormal electrical discharges in the brain which lead to seizures

Ethical – having to do with right or wrong

Ethical review process – a system for determining whether research is ethical

Gene therapy – treating a disease by correcting faulty genes in a patient's cells

Haemorrhage – an uncontrolled loss of blood

Humanely – with kindness

Hypothesis – an idea which could explain the known facts and which can be tested by experiment to see if it is accurate or not

in vitro – literally 'in glass'

Insulin – a hormone involved in the regulation of blood sugar

MHRA – the Medicines and Healthcare products Regulatory Agency, an agency of the Department of Health protecting and promoting patient health and patient safety

Morphine (or alternative) – a strong painkiller which can only be prescribed by doctors

Pharmaceutical company – a company which manufactures medicines and carries out research into new medicines

Pharmacological – relating to the study of effects of medicines in the body

Post mortem – an examination of the body after death

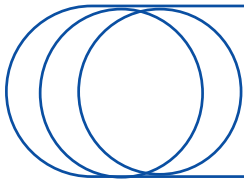
Stroke – a sudden reduction in the blood supply to the brain, usually because of either a haemorrhage or a clot forming, often causing loss of functions such as speech and movement on one side of the body

Synthesised – produced using chemical methods

Therapeutic – helpful in treating illness

Toxicological – relating to harmful substances

Vaccination – giving someone a vaccine, a substance which stimulates the immune system to recognise and attack specific disease-causing organisms



Food for thought

Is it right or wrong to use animals to help find treatments for human illnesses? Would it be right to deny sick people the chance of a long and productive life? Should we have vaccines when they have been researched and developed in animals? What about conditions like migraine which are not medically serious but can be very distressing? There are many rights and wrongs to consider in the complex issue of animal research, and it is only natural to consider different opinions before forming our own.

AGAINST

Animal research is not needed to make new medicines...

FOR

Animal research has been and continues to be essential for the development of new medicines...

FOR

Nobody wants to use animals for research but it would be much worse to let people be ill, in pain or die unnecessarily...

AGAINST

Regardless of the benefits, animal research is morally wrong, there is no justification...

AGAINST

Animals are cruelly treated in UK laboratories. Scientists only care about their research, not the animals...

FOR

Most scientists care a great deal about the animals they use and animal research is strictly controlled by law...

FOR

Animals' and people's bodies are not exactly the same but the similarities are enormous compared to the differences. Provided the research is well designed and conducted, animals give essential guidance about the effects of medicines in people...

AGAINST

Animal research does not help in the development of medicines for people. Animals are too biologically dissimilar to give useful information about the effects of medicines in people. Whatever your moral position, animals are not needed...

Do you believe researchers when they explain that animal research is necessary to develop new medicines? Can we condemn the people who do this work on the one hand, and applaud the results of their work on the other? All of us who have benefited from modern medicine should question every side of the argument.

AGAINST

We would not need research if people took better care of themselves. Prevention is better than cure...

FOR

Prevention is always better than cure. We should prevent illness where we can, and treat it where we cannot...

AGAINST

We can find out all we need to know from careful observation of patients and the identification of factors which lead to illness, along with increased use of computers and cell culture tests....

FOR

Observation in patients provides ideas, not answers. Computer and test-tube research provides some of the necessary information. In addition, scientists need to study the effects of a medicine in carefully designed animal studies. Only then could doctors justify testing medicines in people...

AGAINST

Animal research gives misleading information, making medicines look safe when they are not. This is why medicines have unexpected side effects...

FOR

Animal research gives scientists a good indication of what to expect in patients, so that the human studies can be conducted safely. But even years of these studies involving thousands of patients cannot guarantee that a medicine is safe for everyone...

FOR

Wherever non-animal methods give the necessary information, they are used. The contribution of these methods is increasing all the time but it will be a long time, if ever, before it will be possible to mimic all the functions of a complete living body by computer or in the test-tube...

AGAINST

If scientists really cared about using alternatives, they would have already replaced all animal experiments...



This booklet was produced by the
Animals in Medicines Research Information Centre

part of
The Association of the British Pharmaceutical Industry



Medicines for a healthy future

**The Association of the British
Pharmaceutical Industry**

12 Whitehall
London SW1A 1DY
Telephone: 0870 890 4333
Fax: 020 7747 1411
Email: abpi@abpi.org.uk
Website: www.abpi.org.uk

ABPI Scotland

3rd Floor Crichton House
4 Crichton's Close
Edinburgh
EH8 8DT
Telephone: 0870 890 4333
Fax: 0131 225 4865
Email: abpi@abpi.org.uk
Website: www.abpi.org.uk

ABPI Cymru Wales

2 Caspian Point
Pierhead Street
Cardiff Bay CF10 4DQ
Telephone: 0870 890 4333
Fax: 02920 454 298
Website: www.abpi.org.uk