

All pharmaceuticals have to be tested

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All pharmaceutical medicines have to be licensed before they can be sold. This means they have to be thoroughly tested for safety and effectiveness.

Pharmaceutical testing

National and International standards

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To be sold in Europe medicines have to be approved by the European Medicines Agency (EMA), and in the USA by the Federal Drugs Administration (FDA).

Pharmaceutical testing

How are new medicines tested?

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To obtain approval, a very stringent testing procedure must be followed. It takes many years and is very expensive. Only the few drugs which pass the tests are allowed on the market.

Pharmaceutical testing

Pre-clinical trials, using animals

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Before medicines can be tested on humans, they must usually be tested for effectiveness and toxic effects by testing on animals. This estimates a safe starting dose to test in humans, and eliminates some unsafe drugs.

Pharmaceutical testing

Clinical Trials: Four Phases must all be passed

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Phase 0 tests what the drug does in the body. Phase I tests for safety in healthy adult volunteers. Phase II tests sick people compared with a placebo or a similar drug. Phase III tests more people to assess final dose and safety.

Pharmaceutical testing

Side effects

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Most drugs are given by mouth or injection, so it goes to the whole body as well as the organ concerned. This may cause damage or side effects. One purpose of clinical trials is to minimise these effects.

Pharmaceutical testing

Targeted delivery

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New technologies are being developed, e.g. nanotechnologies, which can enable a drug to go just to the specific part of the body where it is needed, reducing side effects.

Pharmaceutical testing

Testing new drugs is expensive

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Testing new drugs takes many years and is very expensive (anything up to €1 billion). The animal testing part is expensive, and pharmaceutical companies are looking for ways to reduce this cost.

Pharmaceutical testing

Timescale for drug testing

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It can take 15 years from starting research to bringing a drug to the market – typically 2 years to set up and identify good drug candidates, 2–3 years for animal tests and 6–7 years for clinical trials.

Pharmaceutical testing

In what medical research are animals used?

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Animals are used in medical research for many purposes, including modeling human diseases, finding out what genes do, and testing potential drugs before testing them on humans.

Animal research in medicine

Animal research is strictly controlled

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Animal research is strictly controlled in EU countries. You must have scientific and ethical approval for the particular research or testing.

Animal research in medicine

Research with animals must be in proportion

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Some animal testing causes suffering to the animal. This has to be in proportion to the benefit expected. It is forbidden to make any animal suffer longer than necessary for the test.

Animal research in medicine

Which animals are used?

A13



Other mammals make the best comparison with humans. Mice and rats are the most common. Sometimes larger animals, like rabbit, dog, sheep and pig are used and, in some cases, primates.

Animal research in medicine

Who can do animal testing?

A14



All animal research and testing must be done in controlled laboratories by trained animal workers under the supervision of an accredited scientist, usually a vet.

Animal research in medicine

Reducing Animal Experiment – the 3R's Principle

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All research involving animals in the EU is subject to the 3R's Principle: Replace by non-animal methods wherever possible. Reduce the number of animals used. Refine the methods to improve animal welfare.

Animal research in medicine

Testing different organs of the body

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Before a drug is used, it must be tested for possible toxic effects in other parts of the body. Tests must be done for heart, lungs, liver, kidneys, reproductive, digestive and nervous systems.

Testing drugs for toxicity

Why not use human cells for testing?

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Ideally human cells could be used for many toxicity tests, but they aren't easily available for all parts of the body. The ESNATS project seeks to solve this by deriving the different cell types from embryonic stem cells.

Testing drugs for toxicity

Can animals accurately represent the human body?

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It is recognised that animal tests may not accurately reproduce human conditions, but they are better than no test at all.

Testing drugs for toxicity

Testing the whole body needs animals

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To test the effect of a drug on the body as a whole it's necessary today to use animals. Mimicking in the laboratory how human organs behave and interact could one day change this, but it's a long way off.

Testing drugs for toxicity

Toxic effects during embryo development

A20



The ESNATS project has developed potential tests, using human embryonic stem cells, to look for toxic side-effects of medicines during the complex development of the human embryo in early pregnancy. This is hard to test by other means.

ES cells for toxicity testing

When to test possible drugs for toxicity?

A21



Animal toxicity tests are expensive and are only done once the best drug candidates are identified. Drug companies would like to do cheaper stem cell tests to screen thousands more chemicals much earlier in the discovery 'pipeline'.

Testing drugs for toxicity

What are stem cells?

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Stem cells are special cells in most body tissues which can either copy themselves, or turn into other cells. e.g. we replace dead skin because skin stem cells constantly make new skin cells underneath.

Stem cells

Embryo and adult stem cells

A23



In the developing embryo, stem cells gradually specialise to produce all the cells of the body. In adult tissue, stem cells exist to keep regenerating particular body cells during the person's life.

Stem cells

Why do scientists use embryonic stem cells?

A24



Scientists can isolate stem cells and keep them indefinitely in the laboratory. Embryonic stem cells are especially useful because they can be turned into many other types of cells.

Stem cells

What happens to embryos used in stem cell research? **A25**



The embryos used for stem cell research are destroyed after the cells have been removed. But these stem cells are kept growing and multiplying in the laboratory indefinitely.

Stem cells

Where do scientists get the embryos from? **A26**



In countries where embryo research is allowed, the most common source of embryos is when couples undergo In Vitro Fertilisation (IVF) and get more embryos than they want to implant. These 'surplus' embryos would normally be destroyed.

Stem cells

Why not get body cells direct from adults? **A27**



Stem cells are found in many adult tissues but are often hard to extract in large numbers. They usually only make cells relating to that part of the body (e.g. bone marrow makes blood cells but not liver cells).

Stem cells

Induced Pluripotent Stem Cells (iPS) **A28**



Scientists have found ways to turn human skin cells back to a stem cell-like state. They hope that these 'iPS' cells can turn into most body cells, without using embryos, but more research is needed to be sure.

Stem cells

Embryonic stem cells are mainly intended for therapies **A29**



The main justification for using embryonic stem cells has been because of their potential to derive cells to treat hitherto untreatable degenerative diseases like Parkinson's, Alzheimer's, diabetes and multiple sclerosis, or severe burns and spinal injuries.

ES cells for toxicity testing

Embryonic stem cells for toxicity tests **A30**



Having created an embryonic stem cell line for therapeutic research, it can also be used to derive different types of body cells to test new medicines for toxicity as an alternative to using animals. This is what the ESNATS project is doing.

ES cells for toxicity testing

Is embryonic stem (ES) cell research allowed in Europe? **A31**



Some EU countries permit no embryonic stem (ES) cell research. Some allow it only with surplus IVF embryos. A few allow embryos to be created for research. Some only allow using ES cells imported from other countries.

ES cells for toxicity testing

Where would toxicity tests using embryonic cells (ES) be allowed? **A32**



Toxicity tests using human cells derived from embryonic stem cells would probably only be used in countries where ES cells were allowed to be used.

ES cells for toxicity testing