

Drug Development

Focus of session:

- understanding the procedures involved in drug trialling and the role of regulatory bodies
- examination of a range of the ‘decisions about science and technology’, including discussion of the ethics of double-blind trials

Resources needed:

- student worksheets 1-3
- scissors

Suggested teaching approach:

1. Get students into groups and give out worksheets 1 and 2.
2. Students cut up the table on worksheet 2.
3. Students discuss the order of phases in their group, then place the 11 phases on paper in the correct order.
4. Discuss the groups’ decisions as a class, getting them to explain the reasons for each phase.
5. Check the correct order before students stick the phases in the left hand column of table on worksheet 1.
6. Give out worksheet 3, and follow the same procedure to get students to match reasons to the phases in their table.

References

Textbook
Chapter 3

Specification
9.3 Medical Ethics

12.5 a-i

Method

Use small group discussion because

- Students enjoy it
- It allows active involvement by everyone
- One loud or quicker thinking student cannot dominate the class
- The shy and less articulate are more able to contribute
- Students learn from each other
- Everyone gets more practice at expressing their ideas
- A two way discussion is almost always more creative than individual thoughts
- Social skills are practiced in a “safe” environment
- It helps individuals clarify arguments for a topic where there are no “right answers”

Phase of development	Reason for each stage of development
Extraction and purification of substance	Isolation of the chemical being tested is important so that it is clear which chemical is the 'active ingredient' of a drug. Sometimes new drugs are synthesised starting with the structure of an existing drug
In vitro testing	The response to the drug of human tissues and enzymes is studied in glass containers
In-vivo testing	A compound which appears not to harm live tissues will now be tested in living animals - most commonly rats and mice. Any effects on all aspects of the animal's health are recorded.
Approval for clinical trials by the Medicines and Healthcare Products Regulatory Agency (MHRA)	The MHRA (an independent body of scientists and doctors) will award a Clinical Trials Certificate if they consider the data from pre-clinical trials shows that the substance passes safety and quality standards. More information on MHRA site under 'our work' http://medicines.mhra.gov.uk/
Application for drug trial to medical ethics committee	Ethics committee advise on the recruitment of volunteers for the clinical trials, and monitor issues such as the payment of volunteers, risk to volunteers, and that a random cross-section of healthy, informed people is being used.
Clinical trials	To test efficacy of drug in humans (i.e. whether it shows a significant effect in treating the target disease), and to test for adverse reactions to the drug in humans.
Phase I Short-term study on effect of drug on a small group of volunteer healthy humans. These volunteers may be given different doses. A doctor closely supervises them.	Confirms if the compound is being absorbed and excreted by the body in the way predicted by Lab tests. Effects of different doses are monitored.
Review of phase I	An independent review of the data collected is made by the Medicines and Healthcare Products Regulatory Agency. The agency recommends proceeding to Phase II trials.
Phase II Phase 1 study extended to groups of several hundred patients.	Results will indicate if the compound has the desired effect in patients with the disease.
Phase III A group of several thousand patients are selected and placed randomly into two groups: 1. The group given the compound. 2. A control group given a dummy compound known as a placebo.	A large group is necessary so that the results can be analysed statistically. If the medicine is effective, then the results will show a statistically significant improvement in the patients receiving the treatment compared with patients given the placebo. It is important that neither the patients nor the doctors know who is having the compound and who is having the placebo.
Data from Clinical trial sent to Medicines and Healthcare Products Regulatory Agency who decide if drug shows a significant benefit to patient compared with placebo.	If the results show a statistically significant benefit for patients, the MHRA will recommend that the drug be licensed. Their role here is that of an independent body examining the trial data.
Product Licence is granted for marketing the drug in the U.K.	

Answers

1. Are the patients healthy?, are they from a particularly vulnerable group (e.g. are they likely to be putting themselves at risk for financial gain, are they able to understand any risk to themselves?), are they taking any other drugs?, have they recently had an illness which may affect their reaction to the new drug?, is the risk to the volunteer worth the potential benefit of the drug? etc.
2. If the payment made is too large, the motives of the volunteer may include financial gain. This may result in vulnerable people agreeing to volunteer even though they would rather not take part.
3. Their independence should make sure that decisions made on the suitability of the drug are not affected by any vested interest in the drug's success.
4. If doctors involved in the trial knew which treatment their patients were receiving, this could affect the result of the trial. It would be very difficult for doctors not to give out the drug in such a case. The trial results would then be invalid, so the trials must be double blind.

The necessity of double-blind trials to remove the effects of 'expecting a particular outcome' means that the doctor is removed from having to make his decision. For a particular individual, receiving a placebo treatment may well be putting them at risk because they are then not being treated for the disease. This is one of the reasons why it is important to explain the procedure carefully to volunteers.

5. The patient's immune system may be able to fight off the disease without help from the drug.

The patient may be benefiting from the attention of the trial doctor, e.g. time to talk about their illness and ask questions reduces anxiety.

Drug development

The constant development of new drugs in order to compete with new forms of disease, and to attempt to improve on existing drugs, requires a well-defined testing procedure.

In this activity you are asked to decide on the sequence of the procedures that need to take place, from the discovery of a new substance to be tested, to the marketing of a drug passed safe for prescription.

1. Cut up the table on worksheet 2.
2. Discuss in your group to decide on the correct order for these phases. Place the 11 phases on paper in the correct order.
3. When you have decided on the order, discuss this as a class, with the reasons for each phase and check with your teacher that you have the correct order.
4. Stick the correct phases in the left hand column of the table in worksheet 1.
5. Now place the cut up 'reasons for development' from worksheet 3 in the correct position in the second column. Discuss with your group, and check before you stick these in.

Student worksheet 1

Reason for development						
Phase of development						

Reason for development						
Phase of development						

Questions

1. You are on the ethics committee for the trial of a new drug. A company comes to you with the results from pre-clinical trials of a new drug, and wanting to go on to clinical trials. What questions will you ask?
2. Why may you want to reduce the payment to volunteers for the clinical trials?
3. Why is it important that the Medicines and Healthcare Products Regulatory Agency is independent of the drug company?
4. If a patient is seriously ill from the disease that the new drug is expected to treat, should the doctor conducting the clinical trials attempt to make sure that this patient receives the drug rather than the placebo? Is it unethical for the doctor not to treat the patient with the drug in this case?
5. Suggest why patients on a placebo will sometimes show an improvement in their condition.

Student worksheet 2

Drug development

Cut up these sections which are phases in the development of a drug.

<p>Phase I Short-term study on effect of drug on a small group of volunteer healthy humans. These volunteers may be given different doses. A doctor closely supervises them.</p>	<p>Data from Clinical trial sent to Medicines and Healthcare Products Regulatory Agency who decide if drug shows a significant benefit to patient compared with placebo.</p>
<p>Application for drug trial to medical ethics committee</p>	<p>Extraction and purification of substance.</p>
<p>Phase II Phase I study extended to groups of several hundred patients.</p>	<p>In-vivo testing.</p>
<p>In vitro testing</p>	<p>Product Licence is granted for marketing the drug in the U.K.</p>
<p>Clinical trials</p>	<p>Approval for clinical trials by Medicines and Healthcare Products Regulatory Agency.</p>
<p>Review of phase I</p>	<p>Phase III A group of several thousand patients are selected and placed randomly into two groups: 1. The group given the compound. 2. A control group given a dummy compound known as a placebo.</p>

Student worksheet 3

Drug development

Cut up these sections which are reasons for development

<p>To test efficacy of drug in humans (i.e. whether it shows a significant effect in treating the target disease), and to test for adverse reactions to the drug in humans.</p>
<p>If the results show a statistically significant benefit for patients, the Medicines and Healthcare Products Regulatory Agency will recommend that the drug be licensed. Their role here is that of an independent body examining the trial data.</p>
<p>Isolation of the chemical being tested is important so that it is clear which chemical is the 'active ingredient' of a drug. Sometimes new drugs are synthesised starting with the structure of an existing drug.</p>
<p>Results will indicate if the compound has the desired effect in patients with the disease.</p>
<p>Confirms if the compound is being absorbed and excreted by the body in the way predicted by Lab tests. Effects of different doses are monitored. A review of the data collected is made by the UK Medicines and Healthcare Products Regulatory Agency. The agency recommends proceeding to Phase II trials.</p>
<p>A compound which appears not to harm live tissues will now be tested in living animals - most commonly rats and mice. Any effects on all aspects of the animal's health are recorded.</p>
<p>Ethics committee advise on the recruitment of volunteers for the clinical trials, and monitor issues such as the payment of volunteers, risk to volunteers, and that a random cross-section of healthy, informed people is being used.</p>
<p>The MHRA (an independent body of scientists and doctors) will award a Clinical Trials Certificate if they consider the data from pre-clinical trials shows that the substance passes safety and quality standards. More information on MHRA site under 'our work' http://medicines.mhra.gov.uk/</p>
<p>A large group is necessary so that the results can be analysed statistically. If the medicine is effective, then the results will show a statistically significant improvement in the patients receiving the treatment compared with patients given the placebo.</p> <p>It is important that neither the patients nor the doctors know who is having the compound and who is having the placebo.</p>
<p>The response to the drug of human tissues and enzymes is studied in glass containers.</p>
<p>An independent review of the data collected is made by the Medicines and Healthcare Products Regulatory Agency. The agency recommends proceeding to Phase II trials.</p>