



Discussion Continuum 1:

Who pays to develop drugs?

Introduction:

The process from the research into a new drug and its arrival onto the shelves of pharmacists is long and complex, and involves significant investment. This resource gives young people the opportunity to investigate ethical, legal and socioeconomic issues around the drug discovery and development process, such as drug testing, marketing investment, and the effects of globalisation, and asks them to consider a number of statements and situations surrounding the costs of drug development, and the investment on rare diseases.

Groups of 8-11 people discuss the issues raised by each statement and agree where each card should go between 'agree' and 'disagree'. Larger groups could use the resource to have a free discussion of the topic or you could use formats that require the students to work more formally or in smaller groups.

Contents:

The resource consists of:

- An AGREE and a DISAGREE card
- 11 Discussion Cards, which include a statement on some aspect of drug development and if appropriate some further information

- 5 Info Cards, containing more detailed information on elements referred to by the discussion cards

Gameplay:

1. Players form small groups, up to 11 per group. Each group is given an AGREE and DISAGREE card and 11 discussion cards.
2. Within each group, the AGREE card and DISAGREE card are placed on the floor/table about one metre apart, to represent the two extremes of the continuum. The space in between is where the discussion cards will be placed.
3. The first player reads the first discussion card to the rest of the group. The player should check everyone understands the card, and use Info Cards where necessary to ensure the group understands the statement.
4. The first player then decides to what extent s/he agrees with the first card. S/he places the card face up, anywhere on the discussion continuum, closer to AGREE or DISAGREE as s/he chooses. This is entirely the choice of the individual player, and is not discussed by the group. The player can give a reason, if s/he wishes.
5. Each player in turn then reads a card, checks that everyone understands, and chooses individually where to place it on the continuum in a similar way.
6. When all the cards have been read, understood and placed on the continuum, the discussion begins. The aim is to place the cards between AGREE and DISAGREE in an order that most of the players agree on. Players should pick a card for discussion, and debate whether to move it.
7. At the end of the discussion, each group should have a continuum which they mostly agree with.
8. If several groups are playing at the same time, the facilitator may wish to bring the different groups' results together. Are they similar? Can someone from each group explain their choices on particular cards?

Discussion continuum developed by Ecsite, in collaboration with Barcelona Science Park, in the context of the Xplore Health project.

Thanks to At-Bristol for the development of the discussion continuum format: www.at-bristol.org.uk

Agree

Disagree

Discussion cards

Text in bold is the “statement” which the player can agree or disagree with. Text in italics is additional information. For even more additional information, players can refer to Info cards.

“The government has a limited budget for research and development of new drugs. For rare diseases, the government should spend less money for the research of new drugs.”

The drug discovery and development process takes an average of 10-15 years from idea to drug in the market, and costs around 600 - 800 million euros. For more information, see Info Card A.

“Adverts and marketing for pharmaceutical drugs should be banned, as they make drugs expensive. Information about medicines available should come from the government via doctors, not from private companies.”

Pharmaceutical companies who want to promote the use of their approved new products usually approach medical doctors to highlight the benefits to patients of the use of their pharmaceutical drugs. For more information, see Info Card B.

“Doctors should be encouraged to prescribe brand-name drugs, rather than generic drugs, in order to ensure pharmaceutical companies can make enough money to keep costs low.”

Generic drugs contain the same active ingredient as brand-name drugs but at a much lower sales price. For more information, see Info Card B.

“Pharmaceutical companies should be forced to declare all the costs related with developing a new drug – research, testing, registration, approval and marketing. This way it is clear whether or not they are making their prices too high.”

For more information, see Info Card C.

“When a drug is under development and being tested, the researchers who perform the tests should be funded by the same pharmaceutical company which will sell the drug.”

For more information, see Info Cards A and B.

“When a drug is being tested, the company developing the drug should be obliged to report the results of all tests, not just the ones where the result showed the drug is effective.”

For more information, see Info Card B.

“If you want to know what the side effects of a medicine are, you usually have to read a lot of small print. Drug manufacturers should be obliged to print the commonest side effects clearly on the front of the packet.”

“Governments should reward pharmaceutical companies with tax reductions if they develop drugs against rare diseases, as these drugs are expensive to produce and will not be bought by many.”

A rare disease is a disease which affects less than one person in every 2,000 people. Treatments for rare diseases are known as orphan drugs – see Info Card D for more information.

“The government of each country should focus the health budget on developing drugs for the diseases which are most common in that country.”

See Info Card E for more information.

“If a new treatment is found for malaria, the governments of developing countries should respect international patenting laws, and should not be allowed to develop a generic drug until the patent has expired.”

When a new drug is developed, it gets a patent to prevent generic alternatives entering the market until the patent expires, and thus maintains high prices for medication. For more information, see Info Card E.

“Pharmaceutical companies in Western countries should not be allowed to test drugs on volunteers from developing countries, where people are more likely to accept tests because they can’t find any other treatment for their disease.”

See Info Card E for more information.

Info Card A:

Drug development process

The drug discovery and development process is long (an average of 10-15 years from idea to drug in the market), and very expensive (around 600 – 800 million euros). Many drugs have been developed during the last 100 years, for a large variety of diseases. These drugs are usually either chemical compounds, made in the laboratory, or extracted from natural sources; or biological entities (proteins, antibodies, etc.) produced in biotechnological laboratories.

Public-private partnerships

Pharmaceutical and biotech industries partner with academic researchers. The first steps in Drug Discovery research are often carried out by interdisciplinary teams: chemists, biologists and computer technologists.

Structure-based drug design

Genomics (the study of the human genome, and that of other species) allows scientists to find molecules in our body that may be associated with particular diseases. With computers, they can analyse how chemical or biological entities will interact with these molecules, and design future drugs.

Testing

Compounds which show signs that they may be effective are tested in the laboratory in vitro. If they pass these tests, to become drugs for humans, it is first necessary to analyse their effects on animal species. These tests are highly regulated so as to limit the number of animals treated, and need to be approved by ethical committees. Drug approval agencies require that tests carried out in animals are included in each drug dossier.

Drug safety profiles are carried out in cells, so that possible adverse interactions may be found, and the most effective and least toxic compounds are selected.

These compounds are then produced in large amounts, and any impurities are tested. They may be approved for human testing only when its impurities are below a certain safety level, and tested for toxicity. They also have to be prepared in a way so they can be safely administered to humans.

There are then three phases of clinical tests on humans (see Info Card B).

Source: How are drugs developed? Ethical, legal and social aspects. Dr. Albert Royes, Dr. Jordi Quintana www.xplorehealth.eu

Info Card B:

Clinical testing

Once a compound has passed pre-clinical tests (see Info Card A), all the information is sent to the drug regulatory agencies (in each country or in geographical regions), so that they may approve them for carefully controlled tests in humans.

Phase I: Tests on healthy volunteers

Once approved, a preclinical candidate becomes an Investigational New Drug (IND), which is initially tested in healthy volunteers, to confirm the safety of the compound previously observed in animal tests, in escalating doses in the human species. Possible side-effects of the compounds are tested, as well as levels of compounds in human samples (blood, urine), and how they interact with the human body.

Phase II: Finding the right dose

Once compounds tested in Clinical Phase I have been shown to be safe at different doses, tests are carried out on human patients who have the disease. These tests aim to find the best dose to observe a therapeutic effect, with a minimum of side-effects. In most cases, these Clinical Phase II tests are carried out double-blind: some patients receive the compound analysed, while others receive a placebo (with no effect expected), and neither the people carrying out the tests or the analyses of data, nor the patients, know in which group (drug or placebo) they are.

Phase III: Validation of efficacy in patients

For compounds that are shown to be statistically effective in several patients treated in Clinical Phase II, an effective safe dose is selected for extensive Clinical Phase III studies, usually carried out in a larger number of patients in different countries. A double blind system is applied here as well and, in addition, the efficiency and safety of the compound under study is compared in a blind manner with compounds that may have been previously approved for the same disease.

It is after this Clinical Phase III that a compound effect to treat a disease in human patients is validated.

Source: How are drugs developed? Ethical, legal and social aspects. Dr. Albert Royes, Dr. Jordi Quintana www.xplorehealth.eu

Info Card C:

Marketing new drugs

When a new drug has been developed and tested, a dossier is submitted for approval to regulatory agencies in each country or geographical area (the European Medical Evaluation Agency, EMEA, or the Food and Drug Administration Agency, FDA, for example).

These agencies analyse the documentation and either approve the new drug to enter the market, or request additional tests, or deny approval of the drug, because of lack of efficacy or because of possible side-effects associated with drugs administered to humans.

Finally, if they are approved, the price of pharmaceutical products is usually regulated in each country by the government. Governments can attempt to keep prices low either by enforcing low prices, or by loosening regulations in an attempt to encourage competition.

Patents and generic drugs

When a pharmaceutical company first markets a drug, it is usually under a patent that allows only the pharmaceutical company that developed the drug to sell it. Once the patents protecting a pharmaceutical drug expire (which is usually around 20 years after the patent was filed), the pharmaceutical drugs become generic products, which may be manufactured and sold (usually at lower prices than the original product) by any approved company.

How drugs are marketed

Pharmaceutical and biotechnological companies who want to promote the use of their approved new products usually approach medical doctors to highlight the benefits to patients of the use of their pharmaceutical drugs. In addition, under certain regulations, pharmaceutical drugs are directly advertised to customers through many different marketing channels, a practice that has been controversial, since administration of new pharmaceutical drugs to patients should only be approved by medical doctors.

Some pharmaceutical drugs may be directly distributed to pharmacies by the companies producing them. However, for some products, distribution has to be carried out by hospitals only, because of the need of specialised equipment to administer these drugs.

Info Card D: Orphan drugs



In the European Union, around 30 million people suffer from rare diseases. The EU defines a rare disease as a disease which affects less than one person in every 2,000 people. Because expected sales for drugs to treat rare diseases are small, there is little incentive for drug companies to develop new therapies to diagnose and treat such disorders.

Incentives for orphan drug development

In 1999 the EU unanimously passed the Orphan Medicinal Products Regulation, to encourage industry to develop therapies for rare conditions by giving financial incentives. Orphan drugs are drugs developed for diagnosing and treating rare diseases. In the current system, drug candidates are designated as “orphan” and market authorised through a centralised European procedure. Availability and reimbursement remain a national responsibility.

Although orphan drugs can improve health for millions of people, their high development costs, a small market and marketing exclusivity mean that they tend to be very expensive for the patients and health care systems.

Info Card E:

Effects of globalisation

Developing countries often have less means to develop and manufacture drugs, and so buy them from other countries at the regular market price. Public health in developing countries is often of a lower standard than more developed countries, and citizens tend to have a lower life expectancy.

Patents and developing countries

For some time now, some developing countries, including Brazil, India and South Africa, have decided to bypass the rules of international trade with regard to drug patenting, and have started to produce cheaper generic drugs for serious diseases that are widespread in these populations.

Clinical trials in developing countries

Furthermore, more and more drug manufacturing companies use volunteers from developing countries to conduct their clinical trials. The International Bioethics Committee of UNESCO has warned that this practice is extending because even if these volunteers are financially rewarded, their compensation is very small in comparison to what is considered acceptable in richer parts of the world.

In trials with people who are already suffering from illness, participating in clinical trials is often the only way people in developing countries can get treatment for their disease.

Research into diseases affecting developing countries

A 2001 report from *Médecins Sans Frontières* found that 10% of the world's research on health care is dedicated to diseases that affect 90% of the world's population. The report showed there were no effective therapeutic options or ongoing research for many of the diseases that affect particularly poor countries and their citizens, probably because the investment needed would not be sufficiently profitable for the large companies that develop and market these drugs.

These diseases include malaria, the Human African trypanosomiasis also known as sleeping sickness, Dengue fever, Chagas disease, leprosy, and others that mostly affect developing countries.

Source: How are drugs developed? Ethical, legal and social aspects. Dr. Albert Royes, Dr. Jordi Quintana