**Beating bacteria**

**Beating bacteria activity (version 1)**

Three years ago research started on compounds to kill severe bacterial infections such as MRSA (*Methicillin Resistant Staphylococcus Aureus*). Over 5000 compounds have been tested so far. The project team decided that 10 of these compounds were worth testing further.

The best compound will be used in a clinical trial and be given as tablets to patients who have a severe infection. This experiment will test that the compound is effective at curing the infection. Eventually, if this and subsequent clinical trials are successful your company will apply to the government for a licence so that the medicine can be sold to the health service, and can be prescribed to patients.

As the Project Team you must make a recommendation as to which compound should be used in the clinical trial.

# Activity 1: Finding out what is important

The factors that need to be considered for making a good medicine are explained below.

Use the information to decide which factors are the 3 most important for choosing the new oral medicine to treat bacterial infections. Put your answer on the Memo sheet.

## What makes a good medicine?

These five factors are important in deciding what makes a good medicine.

Potency (strength)

Does it work at a low dose?

Potency indicates how effective the compound is in treating the biological problem. High potency (high strength) means that it works at a very low dose (at a low concentration). For an antibiotic medicine given as a tablet by mouth (orally) the potency needs to be high.

Selectivity

How safe is it?

Some compounds can be very effective, but have unacceptable side effects e.g. headache or feeling sick (nausea). A side effect is anything other than the useful and desired effect of the medicine.

All medicines have side effects, however small. The aim is to select the compound that works the best (high potency score) whilst having the least side effect score. The higher the selectivity the better.

Solubility

How well does it dissolve in water?

The compound must have some solubility in water (however small). This is important because living cells are made of water, and are bathed in a watery solution. A medicine will only reach cells and work on them if it is soluble. This is important if the medicine is to be given by mouth (orally) since the stomach and intestine are watery, or by injection since the blood is watery. It is not so important if the drug is given directly on to the surface of cells such as skin creams or inhaled drugs. Most compounds have got enough water solubility to work orally.

Bioavailability

How much gets into the blood stream?

Compounds given orally are taken up into the blood stream from the stomach or small intestine. The amount that is taken up varies from drug to drug. Bioavailability shows what proportion of the compound reaches those parts of the body where it needs to work after it has been given orally. Bioavailability is very important if the medicine is to be given by mouth (orally).

Ease of Formulation

How easy is it to make a tablet or a powder for inhalation?

The physical properties of the compound are very important. They determine how easy it is to make it into a tablet or into a solution for injection etc. For example, big crystals dissolve much more slowly than fine powders. Although this is a very important factor for oral medicines most solids can be ground up to give fine powders.

Now decide on the 3 most important factors for choosing the new oral medicine to treat bacterial infections. Put your answer on the Memo sheet provided.

# Activity 2: Finding the best compound

As a project team you need to decide which of the 10 compounds is the best to take forward based on the 3 factors that you decided were most important in Activity 1.

Use the data below to help you choose the best compound to take forward and develop as a good antibiotic oral medicine. Put your answer on the Memo sheet.

### Data

The table shows the results from the 10 most promising compounds (A to J).

They are all compared to the best compound being used at the moment called “the standard”. This is being used in an experimental trial in a specialist clinic for patients with infections. The standard works but there is room for improvement. It is not generally available to doctors and patients.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Compound | Potency  P | Side effects  S | Selectivity  P ÷ S | Solubility | Bioavailability | Ease of formulation |
| A | 79 | 0.50 | *158* | ★★ | ★★★★ | ★★★ |
| B | 40 | 1.58 | *25* | ★★★★ | ★★★ | ★★★ |
| C | 250 | 1.00 | *250* | ★★★ | ★★ | ★★★ |
| D | 20 | 0.63 | *31* | ★ | ★★ | ★★★★ |
| E | 200 | 1.26 | *159* | ★★★ | ★★★ | ★★★ |
| F | 25 | 0.79 | *32* | ★ | ★★ | ★★★ |
| G | 71 | 0.71 | *100* | ★★ | ★★ | ★★ |
| H | 123 | 0.33 | *373* | ★★ | ★★★ | ★★★ |
| I | 51 | 0.12 | *425* | ★★ | ★★ | ★★★★ |
| J | 16 | 1.30 | *12* | ★ | ★★★★ | ★ |
| *Standard* | 1 | 1.00 | *1* | ★★ | ★★ | ★★ |

Potency: the number shows how many times better the compound is when compared to the standard:

For example, the number for compound E is 200. This means that compound E works at 1/200th the concentration of the standard; it is 200x stronger.

Side effects: the number shows how the compound compares with the standard. For example:

2.0 means that compound is worse than the standard – twice as bad

0.5 means that compound is better than the standard – twice as good

Key to **solubility**, **bioavailability** and **ease of formulation**

★★★★ good ★★★ average ★★ below average ★ poor

Selectivity is the ratio of the potency score divided by side effect score.

Now decide on the best compound to take forward and develop as a good antibiotic oral medicine. Put your answer on the Memo sheet.

## Activity 3: Manufacturing and launching the new antibiotic medicine

Read through the information below.

Decide whether it will be quicker for your company to make the stock for the launch itself, or to place an order with another UK manufacturer. Put your answer on the Memo sheet.

## Part 1: Manufacturing the new antibiotic medicine

The manufacture of the new antibiotic medicine involves three stages:

• Buying and receiving the raw materials

• Manufacturing the chemical compound from the raw materials

• Making up the new antibiotic medicine from all the ingredients (including the chemical compound) and packaging.

The stock needed for the launch is 4 million packs.

The raw materials are readily available from a Japanese supplier. It takes 4 months to get this raw material from the time of placing an order.

1. You could contract out the whole manufacturing process to another UK company. They could deliver the stock 10 months after receiving the raw materials.

2. Alternatively your company could manufacture the new treatment itself. However, you would need to buy a special monitoring device to be used in the chemical manufacturing stage. This is only available from an American supplier. The device will take 6 months to arrive from the time of order.

If your company manufactures the new antibiotic medicine, it will take:

2 months (after receiving all the raw materials) to make the chemical compound

then 4 months to produce the launch stock

Now decide whether it will be quicker for your company to make the launch stock itself, or place an order with another manufacturer. Put your answer on the Memo sheet.

## Part 2: Launching the new antibiotic medicine onto the market

Decide on the launch date for the new medicine using the information below. Put your answer on the Memo sheet.

Before you can launch the new antibiotic medicine you must consider the following stages. These can only happen one after the other.

• Testing in the laboratory should be completed by the end of next year.

• Clinical trials in healthy volunteers and patients suffering from infections (both adults and children) will take four years to complete.

• The treatment must be registered with the authorities in the country where it will be launched first. This will take 1 year.

• As soon as the treatment has been registered, the raw materials will be ordered and the launch stock manufactured. Use your answer from Activity 3 to decide how long this will take.

Now decide:

When to launch the new antibiotic medicine

What to call it

Put your answers on the Memo sheet