



Wellcome Film Project

Retrovir Introduction at Dartford

Wellcome Trust Foundation, 1986.

Colour

Duration: 00:07:26:24

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<Unnamed female narrator, over various shots of Retrovir production at Dartford>

The introduction of a new pharmaceutical entity onto the market is a complicated process requiring considerable work. Reactions that transform raw material into active ingredients under carefully controlled laboratory conditions are scaled up to industrial proportions. How will they work on a large scale? How tightly controlled must they be? The active drug must be made up so that it can be presented to patients. Will tablets, capsules or liquid be best? And in what dosage?

Formal testing procedures, standards and specifications for the raw materials, active ingredients and final product must be established. Protocols are prepared for regulatory authorities, and commercial decisions present themselves. What is the marketing strategy? Will the drug be released worldwide or territory by territory? What about packaging, support materials and so on? The company must establish the supply of raw materials for manufacture and how to store and distribute the active intermediaries and final product.

Introducing a drug normally takes years. With Retrovir it was a different story. On September 19th 1986, a double-blind clinical study to examine Retrovir was stopped because it was obvious the drug was defective in reducing mortality in patients. Wellcome decided that its introduction was a top priority.

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The active ingredient in Retrovir is Zidovudine. Zidovudine is manufactured from the basic raw material thymidine by a complex multi-stage process.

Barry Alcock works in Primary Manufacturing at Dartford.

<Barry Alcock to camera and over various shots of Retrovir production at Dartford>

In September 1986, we began to investigate the process and to investigate the plant requirements for that process to enable us to begin manufacture in January 1987. This involved quite major modifications to our existing plant; the unique thing about the plant is that we try to keep it as flexible as possible so that we can reconfigure it to cope with different products, and that enables us to make a wide variety of different chemicals in the area. We needed a massive amount of engineering work to actually enable manufacture to begin in January. Staff from the chemical division, engineering divisions and the development laboratories were all brought together in project teams to co-ordinate all the efforts. Most of the engineering work was completed by Christmas 1986, but some work did go over the Christmas period and it did require that a lot of people spent most of their Christmas working within the division and didn't get to see a lot of their families.

<Unnamed female narrator>

Zidovudine goes from Primary Manufacturing to Tablet Manufacturing to be put into capsules. Dave Lemon worked on the project.

<Dave Lemon to camera and over various shots of Retrovir production at Dartford>

The decision was made that we would launch on a particular date and then we all moved heaven and earth to make sure that we met that date and that's, in fact I think from the day that was originally given to us, I think we in fact launched a couple of months beforehand. The first we heard of it was last September. It was suggested



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that we would have to go into capsule production. We bought in capsule filling equipment, capsule weighing equipment and capsule banding equipment. We had to get that very very quickly, the normal lead time has been about 6 months, and in most cases the equipment was delivered within 3 months. We then had to commission it and then get it going so there were a lot of hours put in by everybody – engineering staff and so on, we had to build new areas even.

I think everybody got involved in it with a good will, that's from the operators upwards, they all assisted, they all helped; because it was new equipment it was the most modern equipment that was available and that helped as well.

00:03:59:04

<Unnamed female narrator over various shots of Retrovir production at Dartford>

Because of the urgency, production of capsules went ahead immediately. Doug Faulkner of Quality Assurance.

<Doug Faulkner to camera and over various shots of Retrovir production at Dartford>

We had to get the process right first time, on the first production batch and this involved a great deal of analytical input on our part. The first batch involved something of the order of 300 analyses, through from the blend, in process samples, through to the final sample. The product had to meet the final specification and that's exactly what it did do.

<Unnamed female narrator over various shots of Retrovir production at Dartford>

All paperwork related to Retrovir was given special treatment.



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<Jeff Waddingham to camera and over various shots of Retrovir production at Dartford>

Everything was put through on the 'no queue' system which meant that as soon as somebody received a bit of paper with 'Retrovir' on it, it had to be actioned and passed on down the chain.

With our thoughts on flexibility, we just designed the 1 single pack in the English language which we wanted to be suitable for all the world requiring sales packs. For countries where an English language pack was unacceptable, they could put a local language label on the side of the carton.

The company went out of its way to ensure a fair distribution system. To do that we worked on figures published by the World Health Organisation, and very loosely the allocations were just derived at from the amount of drug available, in the UK and Wellcome USA, company policy has been though that once a patient is started on Retrovir they will continue to be supplied with that drug.

<Unnamed female narrator over various shots of Retrovir production at Dartford>

Wellcome are proud of the team effort that went into bringing Retrovir to the market. By investing in the latest technology and making full use of computerised equipment, we now have sufficient capacity to meet foreseeable demand for this product through normal distribution channels.

It usually takes at least 3 years to get everything right. With Retrovir, the first capsules left Dartford early in March, in 1987, just 6 hectic months after the decision to go ahead with production.

<Jeff Waddingham to camera>



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One would normally expect to work long hours in the office or take work home. With Retrovir it was both and it was continual.

<Barry Alcock to camera>

It was an immense feeling of satisfaction when we saw the first material coming off the production line as it were. There was quite a crowd of us there, gathered around to have a look at it – none of us really knew what it looked like and there were a few cheers went up when we made the first batch.

<Doug Faulkner to camera>

It was a tremendous challenge, because of deadlines and because of the very fine limits which we had to meet, yes, it was enjoyable.

<End credits >

Throughout Wellcome, many dedicated professionals made the introduction of Retrovir a success. The company would like to thank them all.