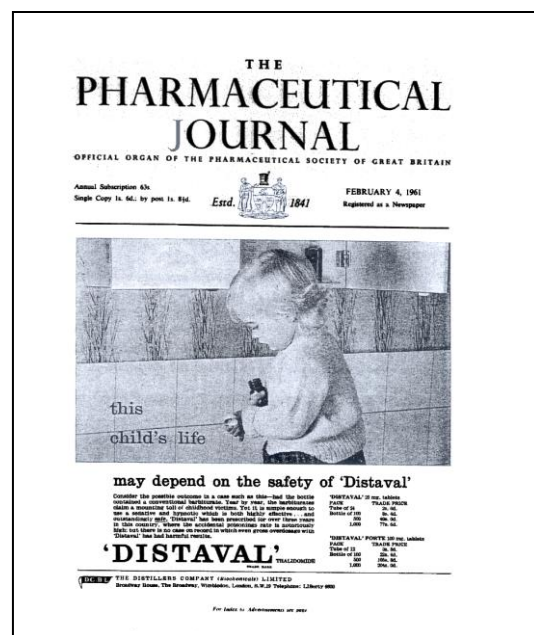


Thalidomide was originally synthesised by Ciba in 1952: it was found to have no effect on animals and was discarded. In 1957 it was acquired by Chemie-Grünenthal in Germany. Further tests were carried out in animals, and in 1958 it was marketed as an anticonvulsant for the treatment of epilepsy in humans. It was of limited value for this purpose, but it was found to be effective at inducing sleep.

It was then marketed as a sedative and tranquilliser; it had a prompt action, and produced natural sleep with no hangover. In 1959 it became Germany's most popular sleeping tablet. It was sold without prescription, and it was cheap and effective.

In 1959 the Distillers Company obtained the rights to market it in the UK and throughout the Commonwealth. As its use grew side effects began to be reported. In 1960 the first neuropathic side effects were reported in an article in the *British Medical Journal*. And in 1960 several cases of phocomelia, a previously rarely seen congenital malformation of the limbs, were reported; little notice was taken of these since no link had yet been made with thalidomide.

In 1961 the reports of peripheral neuritis were mentioned for the first time in company literature. The drug was made prescription only in Germany. In September 1961 a sudden increase in cases of phocomelia were reported. A German paediatrician, Wonderkind Lenz, noted that 50% of these patients had taken thalidomide. In October 1961 Grunenthal were warned of the problem.



On 20 November 1961 an announcement was made at a paediatric meeting in Dusseldorf. A few days later Grunenthal withdrew the drug from the market. On 28 November 1961 a statement was issued by the UK Ministry of Health warning patients to stop taking the drug. Up to 5,000 deformities in UK; 10,000 worldwide

Immediate response to the thalidomide disaster

The disaster triggered a response by many organisations. In July 1962 the College of General Practitioners set up a Register of Unexpected Toxicity. In August 1962 the Association of the British Pharmaceutical Industry set up an expert committee on Drug Toxicity chaired by Dr R Hennessey of the Wellcome Foundation. And in August 1962 the government's Standing Medical Advisory Committee set up a joint sub-committee on the safety of drugs, chaired by Lord Cohen.

In March 1963 the Cohen Report published its final recommendations, including one suggesting that all new drugs and preparations should be submitted to a Committee on the Safety of Drugs, having 4 sub-committees, on toxicity, clinical trials, therapeutic efficacy, and adverse reactions. The Cohen Report also expressed concern about other areas of drug safety that were **not** covered in the committee's remit:

- the control of the quality of drugs
- control of over-the-counter sales of medicine
- the use of approved names and
- the regulation of therapeutic claims.

The recommendations were gradually implemented over the years that followed.

Committee of Safety of Drugs

The Committee of Safety of Drugs (CSD) began work on 1 January 1964. It was established as a voluntary scheme working with the pharmaceutical industry to look at toxicity tests, clinical trials, efficacy & adverse reactions during general use. The CSD established an adverse drug reaction reporting scheme, popularly known as the "Yellow Card Scheme" because the reports were submitted on yellow cards. In the first year, up to 100 reports were received weekly. Nowadays over 20,000 are received annually. Prescription Event Monitoring soon followed, alongside large computing databases, research analysis & the eventual launch of the General Practice Research Database (GPRD) 30 years later.

Medicines Act 1968

Proposals for new legislation to control medicines were published in 1967. These recommended that responsibility should lie with Ministers, advised by a Medicines Commission. The result was the Medicines Act 1968, which brought together in a single Act everything to do with the control of medicines, for both human and animal use, including their promotion and sales. This Act set up the legislation that, as from 1 September 1971, all medicines already on the UK market had to go through peer review and subsequent approval or be withdrawn. This process was ultimately completed in 1990 with only around 5,000 full licences granted out of the original 39,000 products that existed in 1971.

From 1971 all new medicines were subject to pre-marketing assessment for safety, quality and efficacy by the licensing authority. This work was delegated to the Medicines Division of the Department of Health. The Medicines Commission, an expert advisory committee, was set up to advise Ministers. The CSD became the Committee on Safety of Medicines (CSM) and later the Commission for Human Medicines (CHMP).

Other expert committees were also created, including the Committee on Dental and Surgical Materials (CDSM) which completed its work by 1994, and the British Pharmacopoeia Commission (BPC) which continues today. The Veterinary Medicines Directorate (VMD) was established for veterinary medicines.

Today regulation strives to achieve the safety of medicines to the highest standards, achieve an acceptable benefit risk ratio and supply of the correct information to both the healthcare professionals and consumers, without imposing unnecessary regulatory burdens on the pharmaceutical industry. A new threat to public health has however since emerged, in the form of counterfeit medicines.

Thalidomide today

The search for why thalidomide produced the effects it does interestingly led to developments in other forms of treatments using it in such conditions as leprosy and Behcet's disease. Although thalidomide was never originally approved for use in the USA, in 1998 it did gain approval for the treatment of erythema nodosum leprosum, but with very strict restrictions on use and heavy controls. In the UK thalidomide can be used on a named-patient basis but again only under very strict conditions.

FIND OUT MORE

Links to other sheets:

Theme E: The control of harmful substances

Further reading:

Griffin, John P, *The evolution of human medicines control from a national to an international perspective*, (Adverse Drug React. Toxicol. Rev. 1998, 17(1) 19-50 Oxford University Press).

Kayne S B & Jepson M H (eds.) *Veterinary Pharmacy*, (Pharmaceutical Press, London, 2004)

Shah, R R, *Thalidomide, drug safety and early drug regulation in the UK*, (Adverse Drug React. Toxicol. Rev. 2001, 20(4) 199-255 Oxford University Press).