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Arnold O. Beckman, inventor and philanthropist

'There is no satisfactory substitute for excellence.'

The words of Arnold O. Beckman applied to his own numerous achievements during an extraordinary life spanning more than a century. Born the son of a blacksmith on 10 April 1900 in Cullom, Illinois, he went on to have a career that shaped history in the life sciences. The founder of Beckman Instruments, he is widely credited with creating devices that revolutionized the study and practice of human biology and healthcare.

Throughout his lifetime, Beckman wore many different hats, as educator, inventor, civic leader, philanthropist and humanitarian. All these roles were united by his passion for science and a desire to spread the benefits of his own self-made fortune. After reading Steele's *Fourteen Weeks in Science*, originally published in 1861, Beckman set to work converting a tool shed built by his father into a chemistry laboratory using gifts he had received for his tenth birthday. This early foray into science led eventually to a place at the University of Illinois to study chemical engineering. By 1923 he was equipped with a master's degree in physical chemistry, having supported both his studies and family members by playing piano in silent movies.

One of the first high-tech start-up companies

US Patent 2,058,761 has the somewhat plain description of 'apparatus for testing acidity (pH meter)', but few would have predicted the impact this instrument would have on general lab practice. By the time he began working on the pH meter, Beckman had already obtained a doctorate in photochemistry from the California Institute of Technology, where he was also teaching as a professor. While teaching, he was approached by a former classmate who was working for a Southern California citrus processing plant and who wanted a way to measure the acidity levels in lemon juice. 'When you're faced with the necessity to do something, that's a stimulus to invention. If [my classmate] hadn't come in with his lemon juice problem, chances are I never in the world would have thought about making a pH meter.' This device, which made it straightforward to measure acidity and alkalinity, eventually won him a place in the National Inventors Hall of fame in 1987, alongside the likes of Thomas Edison and Alexander Bell.

In 1935, he founded Beckman Instruments Inc – one of the first high-tech start-up companies – in his garage in Pasadena, California. A company of modest beginnings, today Beckman is a multi-billion dollar enterprise and one of the leading manufacturers of instruments and suppliers to the clinical diagnostics and life science markets.

Amongst his seven rules to live by, number seven was 'Don't take yourself too seriously'.

Great inventions

Beckman and his company quickly became the source of many leading instruments and inventions that have shaped human welfare and the biotechnology industry in particular. Beckman was the driving force behind the DU spectrophotometer – a light-measuring device that greatly accelerated the study of chemical and biological reactions. This instrument played a role in elucidating the structure of penicillin – a milestone achievement that enabled synthesis of

Box 1. The seven rules for living of Arnold O. Beckman

- Absolute integrity in everything
- There is no satisfactory substitute for excellence
- Moderation in everything, including moderation
- Hire the best people, then get out of their way
- Don't be afraid of making mistakes; if you are not making mistakes, you're probably not doing very much
- Acquire new knowledge and always ask 'why'
- Don't take yourself too seriously

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the molecule in large quantities.

Further advances included a centrifuge that enabled Jonas Salk to isolate the poliovirus, which was one of the key steps in developing an early vaccine against polio. Instruments from Beckman have also played important roles in screening large numbers of potential drug candidates to treat diseases such as AIDS and cancer. Additional breakthroughs were oxygen analyzers that monitored air composition in incubators to prevent premature babies from going blind due to oxygen deprivation.

In 1982, Beckman Instruments merged with SmithKline Corporation in a deal that was reportedly worth around US$1 billion. The merger catapulted Beckman and his wife into the category of one of the wealthiest couples in California. As such, it marked a stage in Arnold Beckman's life where he devoted himself increasingly to philanthropy. His earlier efforts in this direction had resulted in the foundation of the Arnold and Mabel Beckman Foundation in 1977, an organization that has contributed more than US$400 million in support of scientific research, medicine and education.

A modest, polite and humble man who valued personal integrity, Beckman's achievements were honoured by many awards including the 2004 Lifetime Achievement Award from the National Inventor's Hall of Fame, the 1988 National Medal of Technology, the 1989 Presidential Citizen's Medal, the 1999 Medal of Science as well as the Public Welfare Medal from the National Academy of Sciences.

Arnold Beckman died on 18th May. He was 104.

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An integrated, multidisciplinary approach for drug safety assessment

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This feature article describes a comprehensive approach in drug safety assessment, with which human drug toxicity is evaluated based on the multiple disciplines of pharmacology, chemistry, drug metabolism and toxicology. Mechanistic understanding of drug toxicity and the determination of potential risk factors are proposed to be key parameters for an accurate prediction of human drug toxicity.

One of the major challenges in drug development is the accurate assessment of human drug toxicity. A review by Lasser *et al.* [1] found that, in the past four decades, 2.9% of the marketed drugs were withdrawn from the market due to severe adverse drug effects, with seven drugs approved and marketed since 1993 and subsequently withdrawn to be associated with over 1000 deaths. Lasser *et al.* [1] also estimated that from 1975–1999, 10.2% of approved drugs required black box warnings to be added after marketing. Examples of the recently withdrawn drugs and drugs that required box warnings are shown in Tables 1 and 2, respectively.

The occurrence of unexpected adverse drug effects after a drug is approved and marketed illustrates that the current practice in safety evaluation, although effective in most cases, allows several drugs with unacceptable safety profiles to be marketed. What is particular disturbing is that drugs with undesirable adverse effects are marketed in spite of the estimated US$800 million and 12–15 years in cost and time required, respectively, to develop a single drug [2]. The liabilities to the pharmaceutical industry of market drug withdrawal are obvious, including losses in resources and time spent in drug development, loss in potential revenues and a compromised public image. There is also an ethical issue of causing harm to the patient population.

There is therefore an urgent need to develop approaches to enhance the accuracy of the prediction of human drug safety.

Why can't we predict human drug toxicity?

According to current practice, drug safety is initially evaluated preclinically in laboratory animals, generally in three animal species such as mouse, rat and dog. Preclinical safety study results are submitted to the US Food and Drug

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