employed by the manufacturer or in receipt of consulting fees from the company, claimed that the cardiovascular complications only appeared after 18 months of Vioxx use. This claim was based on a flawed analysis and later formally corrected by the journal that published the report.[4] In the face of numerous subsequent legal challenges from patients, the manufacturer continues to claim that it acted responsibly at all times, from pre-approval studies to safety monitoring after Vioxx was marketed. It has also reaffirmed its belief that the evidence will show that pre-existing cardiovascular risk factors, and not Vioxx, were responsible.[5]

The Vioxx scandal shows that, half a century after thalidomide, there is still much to do to ensure that treatments are tested fairly, that the process is transparent, and that the evidence is robust. As one group of commentators put it 'Our system depends on putting patients' interests first. Collaborations between academics, practising doctors, industry, and journals are essential in advancing knowledge and improving the care of patients. Trust is a necessary element of this partnership, but the recent events have made it necessary to institute proper systems that protect the interests of patients. A renewed commitment by all those involved and the institution of these systems are the only way to extract something positive from this unfortunate affair'.[4]

Avandia

2010 saw another drug – rosiglitazone, better known by the trade name Avandia – hitting the headlines because of unwanted side-effects involving the cardiovascular system. Ten years earlier Avandia had been licensed by drug regulators in Europe and the USA as a new approach to the treatment of type 2 diabetes. This form of diabetes occurs when the body does not produce enough insulin, or when the body's cells do not react to insulin. It is far more common than type 1 diabetes, in which the body does not produce insulin at all. Type 2 diabetes, which is often associated with obesity, can usually be treated satisfactorily by modifying the diet, exercising, and taking drugs by mouth rather than by injecting insulin. The long-term complications of type 2 diabetes include an increased risk of heart attacks and strokes; the main aim of treatments is to reduce the risk of these complications.

Avandia was promoted as acting in a novel way to help the body's own insulin work more effectively and was said to be better than older drugs in controlling blood sugar levels. The focus was on the blood sugar and not on the serious complications that cause suffering and ultimately kill patients.

When Avandia was licensed, there was limited evidence of its effectiveness and no evidence about its effect on the risk of heart attacks and strokes. The drug regulators asked the manufacturer to do additional studies, but meanwhile Avandia became widely and enthusiastically prescribed worldwide. Reports of adverse cardiovascular effects began to appear and steadily mounted; by 2004 the World Health Organization was sufficiently concerned to ask the manufacturer to look again at the evidence of these complications. It did, and confirmed an increased risk.[6]

It took a further six years before the drug regulators took a really hard look at the evidence and acted. In September 2010 the US Food and Drug Administration announced that it would severely restrict the use of Avandia to patients who were unable to control their type 2 diabetes with other drugs; the same month the European Medicines Agency recommended that Avandia be withdrawn from use over the subsequent two months. Both drug regulators gave the increased risk of heart attacks and strokes as the reason for their decision. Meanwhile independently minded investigators uncovered a litany of missed opportunities for action – and, as one group of health professionals put it, a fundamental need for drug regulators and doctors to 'demand better proof before we embarked on mass medication of a large group of patients who looked to us for advice and treatment'.[7]

Mechanical heart valves

Drugs are not the only treatments that can have unexpected bad effects: non-drug treatments can pose serious risks too. Mechanical heart valves are now a standard treatment for patients with serious heart valve disease and there have been many improvements in design over the years. However, experience with a particular type of mechanical heart valve showed how one attempt to improve a design had disastrous consequences. Beginning in the early 1970s, a device known as the Björk-Shiley