Orphan diseases are typically those that are sufficiently rare that there are no commercial incentives to research and develop effective therapies. In order to encourage pharmaceutical companies to invest in orphan drug development, various countries, beginning with the USA, have introduced legislation to provide suitable incentives. Although the definition of what constitutes a 'rare' disease varies from one region to another, there is a remarkable degree of similarity in the incentives provided. These range from market exclusivity for the product in its proposed indication (the most important incentive) to tax credits and reduction or waivers of fees. The USA and Japan also provide sizeable research grants. There is little denying that these measures have had a remarkable effect in meeting the expectations of patients with rare diseases. Among the major pharmaceutical markets, the European Union has most recently enacted orphan drug legislation, in 2000. The success of this legislation has been spectacular and compares well with the first 5 years following the introduction of US legislation. However, scientific advances have outstripped healthcare budgets. Pricing and access seem to vary widely across the globe and are intricately linked with reimbursement. There are inequalities and, in some regions, patients are often faced with having to make difficult choices. There is no doubt, however, that there is greater societal recognition now than ever before that patients with rare diseases are entitled to medicines and, importantly, medicines developed to the same high standard as those for other, more common, conditions.