Introduction

The drug development process typically starts off with a very large number of compounds (i.e. leads). As these are taken through the discovery phase, that number is whittled down, based on pre-clinical data, to identify candidates that are subsequently taken into clinical development. Further attrition occurs during development, until, hopefully, the end-result is an effective licensed product, which brings some benefit to society. The applications discussed in this article take place at the end of the discovery phase and at the beginning of the development phase (see Figure 1a). As drug candidates move through this process, the amount of money spent on each individual candidate under investigation increases — the total cost of developing a new drug is enormous. The earlier an informed decision can be made about which compound to take through to the next step, the better, since resources can then be focused on those candidates with the highest chance of success. This was alluded to in the Food and drug administration (FDA) Critical Path Initiative (1). In particular, there was concern that, whilst over a ten-year period the number of new compounds submitted for registration was declining, the cost of developing a new drug was enormous. The earlier an informed decision can be made about which compound to take through to the next step, the better, since resources can then be focused on those candidates with the highest chance of success. This was alluded to in the Food and drug administration (FDA) Critical Path Initiative (1). In particular, there was concern that, whilst over a ten-year period the number of new compounds submitted for registration was declining, the cost of developing the drugs had more than doubled. As the Critical Path document points out, despite a “revolution in biomedical sciences”, “developers are [still] forced to rely on the tools of the last century to evaluate this century’s advances”, because of the increasing inefficiency of the process. The FDA report highlighted the need to “modernise the critical development path that leads from scientific discovery to the patient”, by adopting and applying scientific advances. That is where Accelerator Mass Spectrometry (AMS) fits in.

The Drug Development Process and AMS Technologies

After a new chemical entity is patented, development work according to the current process may take 10–12 years to reach a point where marketing authority for that compound is granted. This means there is only a relatively short-period of time during which to recoup the investment, before generic copies can enter the market. By using AMS methodology, a human Phase 0 (microdosing) study can be introduced into the drug development process, whereby candidate compounds can be tested in the target species (i.e. humans) before they go into full development. AMS can also be used during Phase I studies to obtain additional information about a compound under development. The early availability of human data can reduce the number of late-stage failures, and can shorten the overall period before the drug reaches the market. Therefore, not only are the medical benefits of the new drug realised sooner, but developers also have more time to recoup their monetary investment (Figure 1b).

What is AMS and how does it work?

AMS was developed in the 1970s, as a technique for radiocarbon dating, and was used to determine the age of archaeological artefacts. It relies on