Abstract. The use of positron emission tomography (PET) in drug development has become more common in the pharmaceutical industry in recent years. One of the biggest challenges to gaining acceptance of this technology is for project teams to understand when to use PET. This chapter reviews the usage of PET in drug development in the context of target, mechanism and efficacy biomarkers. Examples are drawn from a number of therapeutic areas, but we also show that the relative penetration of this technology beyond CNS and oncology applications has been relatively small. However, with the increasing availability of PET
and development of novel radiotracers it is expected that the utilization will be much broader in future years, with the additional expectation that the use of PET as an efficacy biomarker will also become more evident.

13.1 Introduction

The goal of this manuscript is to describe how noninvasive imaging using positron emission tomography (PET) is positioned to significantly impact drug development. In order to best illustrate this opportunity, examples will be given in the context of a biomarker framework (Littman and Williams 2005) that deals with target, mechanism and efficacy applications. It will be clear from this paper that PET (as well as other noninvasive imaging modalities) can be applied at all stages of the pharmaceutical life-cycle.

One of the key challenges to achieving the optimal use of this technique is to ensure that project teams have clearly identified the questions that are faced at a particular juncture in the discovery and development paradigm. With this information in hand, technology groups can identify the range of potential solutions and find the optimal solution, while avoiding the problem of using technology for technology’s sake.

13.2 Biomarker Definitions

There are three definitions of biomarker levels that are commonly used to describe the particular application of a biomarker:

1. Proof of Target (POT)

   In this category, techniques are used to confirm that the pharmaceutical candidate is reaching the desired target in order to confirm the pharmacological mechanism of action. A target biomarker will ideally be able to measure the level of pharmacological inhibition and the duration of action at the target site. In some cases it may be more limited in nature and simply confirm that the drug has reached the target site (for example, brain penetration or tumor uptake). Typically these types of studies are acute in nature and involve looking at changes within a subject from a baseline condition to one following dosing with the candidate pharmaceutical (either single dose or multi-dose).