# How to Succeed in Science

## How to Develop a Clinical Product

### How to develop clinical products: F-18 Florbetaben as an example of molecular imaging development

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Learning Objectives:

- Understand the role of beta amyloid in Alzheimer's disease
- Be able to describe the importance of assay validity and clinical utility
- Be able to describe the critical pathway required by the regulatory authorities in the development of beta-amyloid imaging agents

Development of a successful imaging agent remains a challenging endeavor. Prior to last year no PET agents had been approved since FDG. Recently there has been a great deal of activity around beta-amyloid imaging agents. This provides a unique look at what can be expected for future regulatory approvals. One must show that the agent is binding to the predicted pathologic protein or tissue. For the case of the amyloid imaging agents this meant performing a histology study on end of life patients scanned with the agent during life. After death an autopsy was performed to prove that the signal of the PET agent corresponds to the pathology. The FDA recognized that this may not represent the intended target population. Additional studies may therefore be required in the target population. Emphasis on the ability for the reader to be able to provide a dichotomous yes/no read. The Agency has not yet embraced an approval based on quantitative SUV/SUVR data. For amyloid imaging agents all sponsors have been required to produce a widely accessible training program to read scans. The sponsor must prove that nuclear medicine physicians can access a training program (e.g. web based) that would allow them to have a basic competence of the reading technique without further training or certification. The FDA required validation of the training methodology and a post-marketing commitment to assess reader training under the typical conditions of clinical practice. Although the FDA did not require clinical data assessing the effect of amyloid imaging on clinical management, this has become a sticking point for payers. Reimbursement groups have increasingly required that the results of the imaging analysis be shown to improve patient care. The biomarker hypothesis alone may be sufficient for approval, but not for subsequent market success. Sponsors should consider this early and build it into their development plans.

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