MPR ASSOCIATES INC. ENGINEERS

MPR Rapid Product Development and Commercialization: Case Study on PET Formulation System

Introduction

A positron emission tomography (PET) scan is a unique noninvasive imaging technique that is used to produce three-dimensional images of the living heart, brain or other organs at work. PET scans are often used in the diagnosis and management of cancers, certain brain disorders and heart disease because PET has a unique ability to image complex biological functional processes such as blood flow, oxygen consumption, glucose metabolism, tumor metabolic activity and concentrations of various compounds in selected organs. This is significant because in many cases of cancer when it is first diagnosed or if it has been treated with chemotherapy or radiation therapy, the function of the cells will change before there is any evidence of physical change. As such, conventional imaging techniques may have difficulty identifying cancer at an early stage, or determining if therapy is effective based on anatomy alone. Since PET provides physicians with information about the body's chemistry not available through any other procedure, it is positioned as a complimentary imaging tool to anatomic imaging methods such as CT or MRI scans.

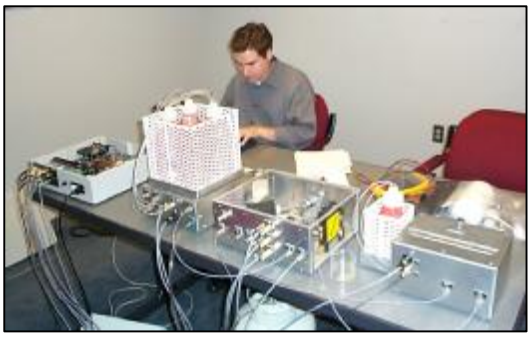
PET imaging is accomplished by injecting a natural body compound, such as glucose, which has been labeled or “tagged” with a small amount of radioactive material. These “radioactive tracers” circulate through the body and emit gamma rays which are detected by a PET scanning machine called a photomultiplier-scintillator detector. The scanner coupled with a powerful computer creates images based on the function of the cells of the body. For example, cancer cells typically use more glucose than the normal cells of the body and therefore collect more of the tracer than normal cells, which allows them to be identified on a PET scan.

PET Formulation System

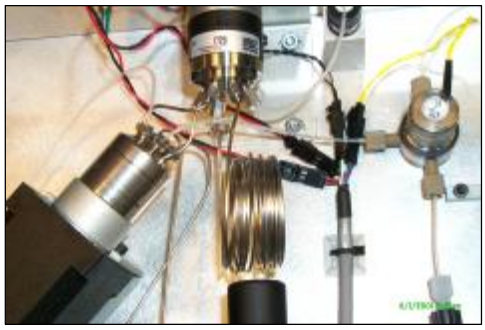
MPR has been working with Washington, D.C. based Bioscan, Inc. for over three years on the development and manufacture of a complete product suite for the automated manufacture of tracer compounds for use in PET imaging studies. Until recently, most tracer compounds have been produced using “homemade” systems developed and pieced together on-site by scientists at research hospitals and other institutions with PET capability. As a result, these systems are typically only able to be run by the creator, are difficult and expensive to maintain, and are not able to produce repeatable, quality, high-radiochemical yield chemical syntheses. This translates into high total cost of production due to the increased waste of expensive chemicals and underutilization of the radioactive C11 lost in a bad batch. Bioscan saw the need in this niche market for a fully automated chemical production system and contacted MPR for help.

MPR's "Auto-Loop" System Development

The initial task for MPR was to begin development on the first of three defined systems as soon as possible to be able to support presentation of a prototype at the largest international industry trade show. This system is called the "Auto-Loop" system, named after the stainless steel coiled HPLC loop where the chemicals are reacted. MPR engineers worked quickly to design and build an initial functional prototype with companion software in just two months, in time for the show.



Proof-of-Concept Prototype



The "Loop"

The design of the system presented several unique challenges stemming from the microliter volumes of fluids being handled and a number of special requirements that had not been addressed well in the "homemade" systems. Specifically, chemical contamination must be avoided throughout the process, the user must not be required to "make-or-break" any fluid fittings during the process, and the system must be thoroughly and automatically cleaned and dried after each synthesis. All of these requirements were met and, in the course of the initial development, a joint patent for the design of the apparatus was documented and applied for internationally. Positive feedback was collected from industry experts at the show and the prototype design was revised and completed four months later. Extensive testing of the final pre-production prototype in the lab showed that the system was remarkably efficient, easy-to-use, and achieved consistently high chemical yields.

Auto Loop Main Module

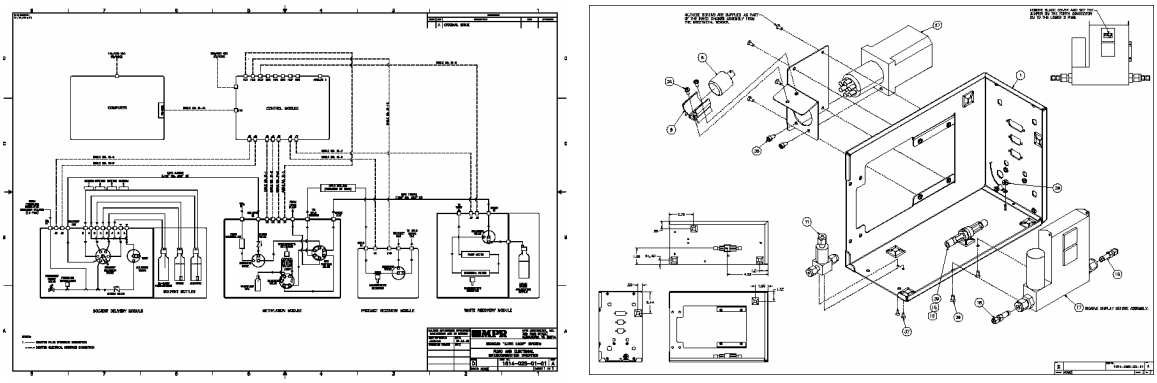
Control & Interface Module

Waste Recovery Module

Reagent Module

System Modules in the Finished Product

The heart of the system is the current Good Manufacturing Practices (cGMP) compliant software which implements an intuitive and interactive graphical interface for performing the syntheses. The software was developed with a specific user in mind, namely, a lab technician with only limited knowledge of the chemistry and the synthesis process. With the process built-in and automated in the software, consistent and reliable runs can be performed back-to-back with little or no oversight by the user. The final system design was captured after minor revisions and a complete manufacturing documentation package was prepared along with software user's guides and installation CDs.



Sample Manufacturing Drawings

System Software and Documentation

The Auto-Loop system is currently installed and in use with great results at twelve labs worldwide. With the rapid success of the Auto-Loop system for Bioscan, MPR started development of the second and third systems in the product line and is currently nearing completion of the pre-production prototypes for those. A fourth system has been added to the product line for which design work is commencing now.

About the Authors

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MPR Associates is an engineering and consulting firm founded in 1964 and headquartered in Alexandria, Virginia. MPR provides technology development solutions for life science firms, with a focus on product design (instruments, delivery systems, devices), manufacturing process development, training, and validation. Key expertise is available in process engineering, fluids handling, mechanical design, materials science, electronics, controls, software, and GMP compliance.

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