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Managing your Radiolabeled Supply Chain in Pharmaceutical Radiosynthesis Life Cycle

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Radionuclide incorporation into pharmaceutical active ingredients continues to be the primary and proven technique to aid the drug development life cycle. Radio labeled drugs assist in understanding drug absorption, distribution, metabolism and excretion. The key advantages of radioactive test articles are the ease of monitoring drug properties through radioactive detection or specified mass.

Radio labels aid drug development from non-clinical to clinical studies with differing levels of compliance based on the stage of development.

Lead compound selection studies may use radio tracers to study investigational drugs and their pharmacological properties, including tissue distribution, specificity and binding properties. These studies range from non-clinical to cGMP.

Typical Pre-clinical Studies and Activities:

- ADME
- QWBA
- Micro dosing
- ^{14}C and ^{1}H starting materials acquisition
- Synthetic route design & lead optimization
- Toxicology studies

Radiolabeling synthesis requires unique understanding of how to assemble molecules, insights into product yields, availability of radiolabeled reagents/starting materials, purification techniques, molecular stability, and label

placement. This knowledge comes singularly from years of experience-thus an "art". Information learned from pre-clinical labeling synthesis will be useful through the life cycle of drug development. Radiolabeling synthetic pathways are often unique and differ from cold routes:

Synthesis technology includes:

- Efficient Synthesis—minimizing synthetic steps, highest yields, limiting waste streams and sourcing radionuclide reagents
- Analytical techniques such as NMR, and MS for characterization
- Separation Technology including preparatory HPLC
- Label placement history
- Full cGMP manufacturing practice—method validation, batch records (view webpage for additional information)

These technologies are also applicable to supply chain of stable label, ^{2}H and ^{13}C, as well as cold synthesis in support of reference materials and metabolites.

The Eurofins BioPharma Product Testing synthesis group and facilities in Columbia, MO, USA has extensive synthesis experience spanning more than two decades with the following attributes:

- Broad scope NRC license including ^{14}C, ^{3}H as well as 19 other isotopes
- Four dedicated cGMP manufacturing suites
- Experienced team of Ph.D.-level synthetic chemists
- Production capabilities up to 500 gram scale – depending on synthesis
- Dedicated analytical support for qualification and generation of certificates of analysis

What are the advantages to keeping radiosynthesis within one group from non-clinical to clinical support?

Technology gained from pre-clinical radiosynthesis may be utilized for cGMP materials, allowing for efficacy and limiting the need for recreating the "art". In addition, an established relationship with a static synthesis team contributes to on-time delivery of test articles.

As a synthesis teams gain knowledge during the initial radiolabeling efforts, this knowledge may be used throughout the life cycle of radiolabeling projects. Keeping synthesis projects with the same team avoids technology transfers, analytical method qualification and transfer, and adjusting to a new organization. Thus knowledge gained in non-clinical synthesis may be leveraged for later stage cGMP labeling. Many times radiolabeled drug supplies are needed in a short time frame, and avoiding transfers but leveraging technical knowledge can save time, minimize budgets and lower risks.

What is cGMP in the Radiolabeling Space?

Today, many clinical sites require confirmation and question the cGMP status of radiolabeled drugs. cGMP is required for drugs entering human subjects and incorporates:

- Following guidance's for introduction of a starting material
- Validation of analytical methodology
- Using cGMP cold material for blending
- Proper documentation including batch records
- Adequately trained personnel

Consider keeping your early to registration radio supply chain with the same team to eliminate time delays, reduce your budget and reduce overall risk.