Stable Isotopes and Medicine (1)

What is a Stable Isotope?
A “Stable Isotope” is any of two or more forms of an element whose nuclei contains the same number of protons and electrons, but a different number of neutrons.

Stable Isotopes remain unchanged indefinitely, but „unstable” (radioactive) isotopes undergo spontaneous disintegration. An „isotopically labelled compound” has one or more of its atoms enriched in an isotope.

Applications
Stable Isotopes are tools used by researchers worldwide in the diagnosis of disease, to understand metabolic pathways in humans, and to answer fundamental questions in nature. They help researchers find answers by allowing them to look at a problem in a new way, from a different perspective. They help to better understand a process, trace a compound from a particular source, measure the concentration of a chemical in a sample, or measure the rate of a related process.

Stable isotopes already play an important role in research today and will become even more important to research in the future.

Positron Emission Tomography (P.E.T.)
Oxygen-18 is a key isotope because it is the raw material for cyclotron production of flourine-18 used in PET (Positron Emission Tomography). Brain function studies use F-18 labelled 2-fluoro-2-deoxyglucose (18FDG) as a tracer.

Isotec has the world’s largest oxygen-18 production capacity, and has been enriching oxygen-18 by cryogenic distillation of nitric oxide since 1985. We offer an abundant supply of this important isotope in a variety of chemical forms with enrichments up to >99 atom%. We supply a wide variety of cyclotron target materials such as water-18O, nitrogen15N/oxygen gas mixes, and carbon-13C (amorphous), and maintain an inventory of the most commonly requested products for rapid delivery.

The enrichment, synthesis, and packaging of isotopically enriched oxygen-18 compounds at our own facility give Isotec a distinct advantage in quality control. Controls are in place throughout the production process, including extensive and comprehensive testing of the final product, in order to minimize variation and ensure superior quality.

Magnetic Resonance Imaging (MRI)
Compounds labelled with stable isotopes such as Glucose-1-13C and Glutamic-13C Acid are used in Magnetic Resonance Imaging (MRI) techniques to render visible metabolic change in the brain. The goal of this research is the early diagnosis of neuro-psychiatric disorders.

Researchers are currently exploring the use of helium-3, oxygen-17, and xenon-129 to provide improved lung images. They are also looking at carbon-13 and deuterium labelled products for enhanced imaging of specific regions and the solving of metabolic mysteries. Isotopic labelling provides better resolution and sensitivity than natural abundance in many imaging experiments, and the use of stable isotopes in MRI/MRS techniques is increasing. Isotec provides the highest enrichment and largest selection of stable isotopic products for all MRI applications.

Isotec’s Commitment
Today Isotec is the only commercial manufacturer that separates and enriches over 30 stable isotopes. We have the world’s largest carbon-13, nitrogen-15 and oxygen-18 production capacity as well as substantial noble gas separation facilities. We are involved in all aspects of stable isotope production including the custom synthesis of new and complex labelled compounds. We provide the finest products to researchers in agriculture, biology, chemistry, drug testing, geology, health, nutrition, physics and other fields of scientific interest.
**Stable Isotopes and Medicine (2)**

<table>
<thead>
<tr>
<th>Pharmaceuticals</th>
<th>Breath Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable Isotopes are an excellent candidate for drug substances because they are non-invasive, non-radioactive and safe. The use of stable isotopes as tracer drug substances has increased tremendously in the last decade. Isotec leads in providing stable isotopically drug substances and pharmaceuticals. Our Quality Control Laboratory is committed to developing validated analytical methods in support of raw material procurement, in-process testing and final product qualification. Isotec is committed to following current Good Manufacturing Practices (cGMP). Our manufacturing processes provide for laboratory quality control checks at all critical junctures. This ensures that the highest quality in our products is always maintained throughout the production process. For the first time, stable isotopically labelled compounds are being used on a large commercial scale as pharmaceuticals. We are the first company to successfully meet the US FDA manufacturing requirements for the production of stable isotopically labelled drug substances.</td>
<td>A focus on strategic opportunities in the stable isotope market has helped make Isotec the world leader in $^{13}$C-urea production for the $^{13}$C-urea breath test to detect H. pylory bacteria, recently linked to ulcers. In addition, Campro Scientific provides a wide range of carbon-13 compounds for other breath tests. A few examples are the xylose test for bacterial overgrowth, the triolein test for fat malabsorption, and the aminopyrine test for liver function.</td>
</tr>
</tbody>
</table>

**Custom Synthesis for pharmaceuticals Applications**

Isotec has the most experienced team of custom synthesis chemists in the industry, led by an impressive group of Ph.D.’s, each one an expert in his field. Isotec routinely engages in the multiple step synthesis of complex isotopically labelled molecules including metabolites and steroids. Our on-site production capabilities and inventory of basic starting materials enable us to provide rapid custom synthesis of new compounds. We can deliver your custom synthesis compound faster than anyone in the industry. We will synthesize quantities ranging from milligrams to kilograms and provide custom packaging services. Client confidentiality can be guaranteed.

**Structure Determination of Biomolecules by NMR**

Rational drug design often requires knowledge of the structure and interaction of proteins, RNA or DNA. Isotec provides researchers with a wide range of products used in structure elucidation and new drug development. Modern multiple resonance multidimensional NMR experiments require isotopic enrichment of the proteins, RNA and DNA, to achieve sufficient sensitivity and resolution. The biomolecules are typically enriched by biosynthesis. The bacteria are grown with isotopically enriched nutrients which, in turn, produce a biomolecule of interest that isotopically labelled. The isotopically enriched biomolecule of interest is then purified in readiness for study using NMR. Isotec pioneered large scale commercial production of isotopically enriched nutrients for biological growth of biomolecules. We offer the highest enrichment and chemical purity available for products such as uniformly carbon-13 labelled glucose, deuterium labelled products, isotopically enriched amino acids, and nitrogen-15 enriched ammonium salts, in addition to growth media.

**Nutrition & Metabolic Studies**

Because compounds enriched with stable isotopes are nearly identical to their homologues at natural abundance, applying stable isotopically enriched compounds as tracers is the safest and most effective way of studying metabolism. A large variety of isotopically enriched compounds are used to study the details of metabolic pathways in medicine, agriculture, and basic research. Isotopic enrichment has also become an established technique for determination of metabolic function in plants and animals. Isotec provides stable isotopically labelled products for these applications including the largest variety of carbon, nitrogen, oxygen, and deuterium labelled metabolic intermediates, along with oxygen-18 and deuterium enriched water. We offer sterility and pyrogen testing in addition to custom specifications for customers with special purity and quality control requirements. You can rely on Isotec for the highest quality products because of our in-process testing from isotopic enrichment through rigorous final release requirements.