January 31, 2019

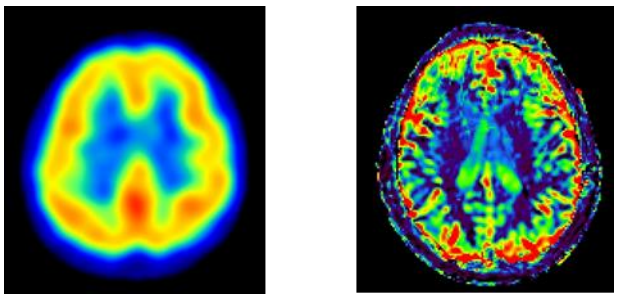
Notice Regarding First Domestic Production and Sales Launch of Water-^{17}O, a Stable Isotope of Oxygen

Taiyo Nippon Sanso Corporation (TNSC) hereby announces that it has succeeded in manufacturing and launched sales of Japan's first domestically produced Water-^{17}O*1, a stable isotope of oxygen, as a research reagent. Water-^{17}O is expected to image important brain function-related parameters such as imaging of brain fluid dynamics, including cerebral blood flow and cerebrospinal fluid.

1. Background

Hokkaido University Hospital has been moving forward on clinical research using Oxygen-17-MRI (^{17}O-MRI) testing*2 for various types of patients. TNSC has been providing the contrast agents (clinical research reagents and investigational products) used in ^{17}O-MRI testing.

In ^{17}O-MRI testing, viewing the dynamics of Water-^{17}O injected as a contrast agent provides clear observation of blood flow and enables testing of such matters as cerebral blood flow and vascular permeability. Compared to nuclear medical scans such as SPECT and PET, ^{17}O-MRI testing provides higher resolution images without exposure to radiation, so it is expected to be used with infants and pregnant women. Furthermore, by obtaining imaging of fluid dynamics not only of cerebral blood flow but also cerebrospinal fluid, it enables elucidation of neurological disorders (Alzheimer's dementia and other cognitive disorders) caused by accumulation of protein wastes in the brain and vastly expands the possibilities of fluid dynamics research within the body.



Img. 1: Left: An image of a brain obtained from a SPECT test
Right: An image of a brain obtained from ^{17}O-MRI testing

(Images courtesy of Associate Professor Kohsuke Kudo, Radiology, Central Clinical Facilities, Hokkaido University Hospital)

2. Production and Sales

TNSC expanded on Japan's third production plant for Water-^{18}O*3, a stable isotope of oxygen, in Yamaguchi Prefecture in 2013 (annual capacity of 300 kg) and started production of Water-^{18}O in 2015. Recently, this plant became the first in Japan to successfully produce Water-^{17}O*1, using a by-product gas. Going forward, TNSC will provide a stable supply of high-quality Water-^{17}O produced under strict quality control compliant with GMP.

1) Product
   ① Product name: Water-^{17}O (research reagent)
   ② Concentration: 10 atom%^{17}O (oxygen atomic ratio)

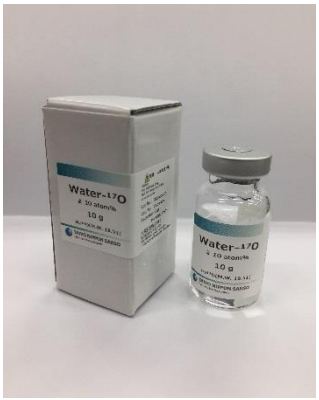
2) Production plant
   ① Production capacity: Water-^{17}O 30 kg/year (10 atom%^{17}O)
   * R&D currently underway to increase and reinforce production capacity
   (Produced together with Water-^{18}O 300 kg/year (98 atom%^{18}O))
   ② Plant location: Shunan Sanso Co., Ltd., Shunan City, Yamaguchi Prefecture

3) Commercialization facility
   ① Features: Production and quality control framework compliant with GMP
   ② Plant location: TNSC SI Innovation Center, Tama City, Tokyo

4) Date sales launched
   February 1, 2019

Img. 2: Water-^{17}O production plant at Shunan Sanso Co., Ltd.

Img. 3: Water-^{17}O commercialization facility at the TNSC SI Innovation Center



Img. 4: Exterior packaging of Water-^{17}O

Glossary

*1 TNSC's Water-^{17}O, a stable isotope of oxygen

A water molecule is a combination of two hydrogen atoms and one oxygen atom, but in Water-^{17}O, the oxygen atom is not the general oxygen atom with a mass number of 16, but water with a stable isotope of oxygen with a mass number of 17.

Naturally occurring oxygen is composed of three types of stable isotopes, ^{16}O, ^{17}O, and ^{18}O, with their ratio (oxygen atomic ratio) at 99.76%, 0.04% and 0.2%, respectively. Physiochemical properties of each of the isotopes are almost identical, making it extremely difficult to concentrate or separate them. TNSC developed an ^{18}O condensation method through an oxygen cryogenic distillation technology and has produced Water-^{18}O with a world-leading concentration of at least 98 atom% since 2004, providing stable supply to PET markets around the world. TNSC has succeeded in Japan's first production of Water-^{17}O through a by-product gas at the Water-^{18}O production plant. Uses are expected to include clinical research such as NMR analysis and ^{17}O-MRI testing uses in the medical sector.

*2 ^{17}O-MRI testing

Magnetic Resonance Imaging (MRI) is an imaging method that uses powerful magnets and electromagnetic waves to obtain images of cross-sections of the body. ^{17}O-MRI testing is a graphic testing method that analyzes changes in MRI signals in response to changes in the degree of concentration of Water-^{17}O within the body.

*3 TNSC's Water-^{18}O

A water molecule is a combination of two hydrogen atoms and one oxygen atom, but in Water-^{18}O, the oxygen atom is not the general oxygen atom with a mass number of 16, but water with a stable isotope of oxygen with a mass number of 18.

TNSC currently has a Water-^{18}O production capacity of 600 kg/year (total of three Water-^{18}O production plants) and provides customers around the world with high-quality products commercialized using production equipment and quality control compliant with GMP. Water-^{18}O is mainly used in medical sectors around the world as the raw material in the PET diagnostic reagent ^{18}FDG.

(^{18}FDG: A PET diagnostic reagent consisting of a fluorodeoxyglucose (a glucose analog) labeled with a ^{18}F positron-emitting radionuclide. ^{18}FDG is accumulated in cancer cells that actively metabolize glucose, so that a PET scanner can use images of ^{18}FDG distribution within the body to diagnose cancer.)