



## Product Description and Specification

| Catalog# | Description |
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**Synthra MeIplus Research with HCN, CO options**

**Synthra MeIplus Research (customized with  $[^{11}\text{C}]\text{HCN}$ ,  $[^{11}\text{C}]\text{CO}$ , options is a flexible and completely automated synthesis system for routine production of wide variety of  $[^{11}\text{C}]$ carbon-labeled compounds based on the generation of gas-phase  $[^{11}\text{C}]$ methyl iodide,  $[^{11}\text{C}]$ methyl triflate,  $[^{11}\text{C}]\text{HCN}$  and  $[^{11}\text{C}]\text{CO}$ . The module allows trapping of  $[^{11}\text{C}]\text{CO}_2$  for Grignard reaction.**

### $[^{11}\text{C}]$ Chemistry

Using in-target produced carbon dioxide, high specific activity preparations are produced ranging from 10 Ci/ $\mu\text{mol}$  to 24 Ci/ $\mu\text{mol}$  when high purity target gas is used for  $[^{11}\text{C}]\text{CO}_2$  production.

#### The target gas should meet the following requirements:

- Cold carbon dioxide ( $\text{CO}_2$ ) content: less than 20 ppb (part per billion)
- Cold carbon monoxide ( $\text{CO}$ ) content: less than 20 ppb (part per billion)
- Cold total hydrocarbon ( $\text{CH}_n$ ) content: less than 50 ppb (part per billion)

The target  $[^{11}\text{C}]\text{CO}_2$  is quantitatively trapped in the stainless steel capillary tubing trap at  $-180^\circ\text{C}$ . After washing out the impurities the  $\text{CO}_2$  is released into the methane oven where it is converted to  $[^{11}\text{C}]\text{CH}_4$  by reduction on a Ni catalyst. The  $[^{11}\text{C}]$ methane is then released and trapped at  $-120^\circ\text{C}$  on Carbosphere<sup>®</sup>  $\text{CH}_4$ -trap and the hydrogen is removed from the system. In a successive gas phase reaction the  $[^{11}\text{C}]\text{CH}_4$  is converted into  $[^{11}\text{C}]\text{MeI}$  and trapped on a Porapak Q filled column.

**$[^{11}\text{C}]\text{Methyl iodide}$**  is ready to be released after only 7 minutes starting from the  $[^{11}\text{C}]$ carbon dioxide trapping. The yield for the  $[^{11}\text{C}]$ methyl iodide formation is  $>50\%$  non-decay corrected. Up to **15** sequential methyl iodide preparations are possible from a single box set-up.

#### Additional $[^{11}\text{C}]$ labeling possibilities

**$[^{11}\text{C}]\text{MeOTf}$ :** The  $[^{11}\text{C}]\text{MeI}$  can be converted to  $[^{11}\text{C}]\text{MeOTf}$  in an additional triflate oven. The conversion yield from methyl iodide is 95%.

Both  $[^{11}\text{C}]$ methyl iodide and  $[^{11}\text{C}]$ methyl triflate can be used for solid support heterogeneous reactions (e. g.  $[^{11}\text{C}]$ choline,  $[^{11}\text{C}]$ methionine) or can be released into the reaction vessel for homogeneous reactions.

**$[^{11}\text{C}]\text{CO}$ :** After the target  $[^{11}\text{C}]\text{CO}_2$  is purified in the trap, the carbon dioxide is released into the Zinc column for catalyzed conversion to  $\text{CO}$ .

**$[^{11}\text{C}]\text{HCN}$ :** The  $[^{11}\text{C}]\text{CH}_4$  is released with  $\text{NH}_3$  gas into the column oven where it undergoes a Platinum catalyzed conversion into  $[^{11}\text{C}]\text{HCN}$ .

**$[^{11}\text{C}]\text{CO}_2$ :** After trapping the target  $[^{11}\text{C}]\text{CO}_2$ , this is directly bypassed into the reaction vessel 1 for Grignard reactions.

Automating the synthesis is simple, with easy-to-use configuration software SynthraView - the Synthra MeIplus Research module offers both, fully automatic and manual modes of operation.

**The module:**

All wetted components are chemically inert, simplifying maintenance and protecting the final product. The customized MeIplus Research is equipped with eleven reagent vials with dead volume free connections to the valves enabling multistep radio synthesis procedures.

The system contains two closed reaction vessels (-196 °C – 250 °C, 1 reaction loop oven (-196 °C – 220 °C) and a cartridge oven (25 °C – 220 °C) enabling multistep reaction synthesis. Both reaction vessels contain heating and cooling function to reduce the reaction time.

The module is equipped with 7 shielded radiation detectors for in-process feedback including the activity of the final radiopharmaceutical preparation as well as four electronic flow controllers.

The synthesis unit has a chemically inert vacuum pump with end vacuum of < 5 hPa (5 mbar) and a liquid nitrogen cooling trap for the collection of radioactive volatiles and for protection of the vacuum pump.

The integrated quaternary gradient Radio-HPLC with a variable wavelength detector includes optional two semi-prep HPLC columns and a switching valve which allows in-process purification steps for different tracer by selecting the column. After HPLC separation a solid phase extraction (SPE) is integrated for a reliable production and formulation of isotonic injectable solutions of [<sup>11</sup>C]compounds with high specific activity.

The module also contains a filter integrity test capability according to GMP. After filtration of the final formulated radiopharmaceutical product, an automated pressure hold test according to GMP is done at the sterile filter. The measuring procedure is monitored and graphically documented.

The synthesizer can be operated either fully automated controlled by software using time lists or by manual operation of the system. The automated as well as the manual operation is performed via graphical user interface.

A laptop for controlling the synthesizer with min. 500 GB hard disk drive, 8 GB RAM, 15,6" screen and LAN port is included. The control hardware is implemented in the synthesizer. The synthesizer is controlled via TCP/IP from the provided notebook.

The synthesizer has program lists for up to 14 different radiopharmaceuticals already built-in. New sequences can be created easily and tested by graphical simulation prior to the operation of the new sequence. The integrated program lists can be used as templates for the creation of new time lists for new radiopharmaceutical productions. The synthesizer has also a built-in cleaning program.

The machine runs with a data logging procedure. All manual or automated operations are separately recorded. The synthesizer provides a synthesis report which includes the preparations steps, the recorded data channels, the yield of the synthesis and the specific activity of the synthesized tracer.

The software generates full GLP conform production documentation including data logging capability. The documentation report includes preparation steps, the graphical trending of the up to 18 channels, radioactivity, temperature and pressure, the radiochemical yield and the specific activity of the labeled radiopharmaceutical. The software has built-in functions e. g. for the preparation and printing of production reports. The software is in full compliance with GMP/GLP guidelines.

A copy of the SynthraView software is provided.

### **Built-in Self-cleaning System**

The built-in fully automatic Self-Cleaning System Option is available for all our systems. The system is equipped with 3 external cleaning solvent supply bottles which are connected to the module through a PEEK manifold and a set of additional valves.

The Self-Cleaning System allows:

- Automatic filling and cleaning program
- Rinse the system after each run without opening the hot cell
- Reduce the dead time between your syntheses

## Features:

### **[<sup>11</sup>C]Gas Phase Chemistry**

- Production of [<sup>11</sup>C]MeI & [<sup>11</sup>C]MeOTf
- 10 to 15 [<sup>11</sup>C]MeI synthesis with one setup
- >50% [<sup>11</sup>C]MeI yield (ndc) in 7 min
- [<sup>11</sup>C]Acetate Option for Grignard reactions
- [<sup>11</sup>C]HCN Option for [<sup>11</sup>C]HCN production and labeling
  - Additional NH<sub>3</sub> flow controller
  - Additional Quartz column with Platinum catalyst
- [<sup>11</sup>C]CO Option for [<sup>11</sup>C]CO production and labeling
  - Additional Zinc column
  - Additional CO trap column

### **Built-in Self-cleaning System**

- 3 external cleaning solvent supply bottles
- additional PEEK manifold
- 15 additional valves:
  - 3 valves for cleaning solvent
  - 1 valve to flush the syringe pump
  - 1 additional valve per the reagent vial
- Fully automated filling and cleaning system
- Multiple cycles possible
- Rinse the system after each run without opening the hot cell
- Reduce the dead time between your syntheses
- Allows two or more [<sup>11</sup>C]productions per day!

### **Heating and Cooling Capabilities**

- Eleven heating zones, six with cooling capabilities (-196 °C - 1000 °C )
- Two closed reaction vessel with integrated cooling to reduce synthesis time
  - -196 °C – 250 °C
  - 2 glassy carbon reaction vessels to choose between the following options:
    - ❖ 3 mL reaction vessel (minimum volume: 50 µL)
    - ❖ 7 mL reaction vessel (minimum volume: 150 µL)
    - ❖ 10 mL reaction vessel (minimum volume: 300 µL)
- Optional loop oven with integrated cooling capabilities
  - -196 °C - 220 °C
  - 800 µL or 1600 µl loop volume
  - 50-70 µL coating volume
- One cartridge and Triflate oven (25°C - 220°C)

### **Cartridge Holders and Reagent Vials**

- 4 cartridge holders
- Seven small (1 - 3 mL) and four large (10 - 15 mL) volume glass vials for reagents
  - valve to select the HPLC column
- 1 SPE Unit

### **Detectors and Controllers**

- Seven shielded radiation detectors for in-process feedback
- Four electronic flow controllers
- Four Pressure sensors
- One built-in filter test unit

### **Dispensers, Valves and Pumps**

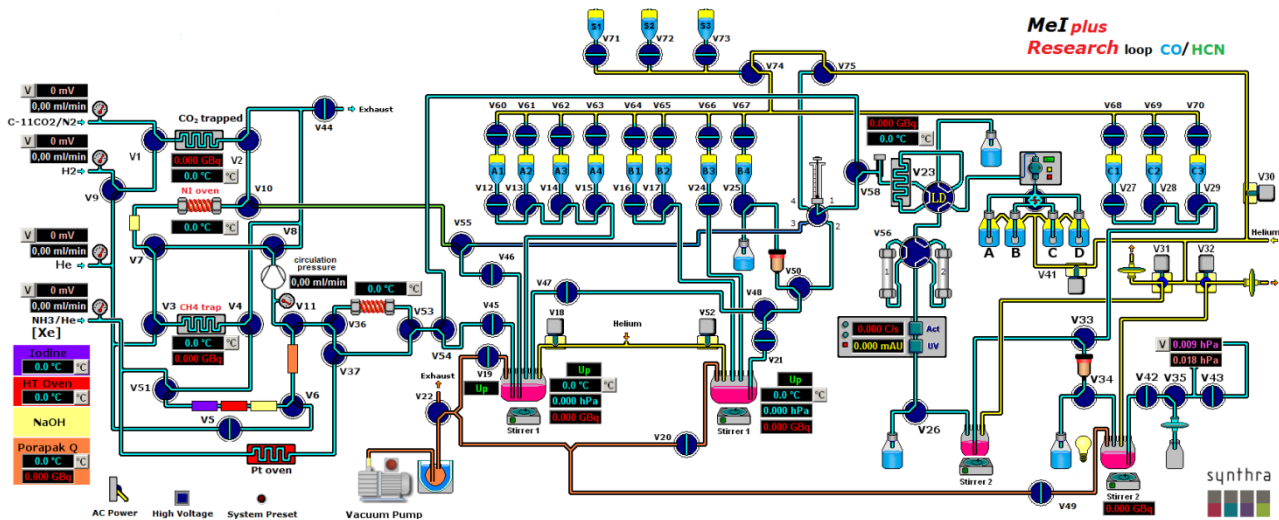
- HR-dispenser (0-50.000 steps, 2.5 or 5 mL)
- HPLC pneumatic injection valve (1.5 - 5 mL injection loop)
- Chemically inert valves with small dead volume (< 35 µL), 5 bar rated
- 10 spare valves for customization
- Chemically inert vacuum pump with end vacuum of < 5 hPa (5 mbar)
- Automatic pneumatic injection valve with a 0.5 to 1.5 mL sample loop

### **HPLC and SPE Unit**

- Built-in preparative Radio/UV-HPLC system (40 mL/min = max. flow) for product collection
  - Variable wavelength detector
  - Quaternary gradient
  - Optional two semi prep HPLC columns for in-process and final purification
- Automatic pneumatic

### **Software**

- User-friendly software easy to set up and operate
- Simple creation of user-defined synthesis methods
- Synthesis files for 14 different radiopharmaceuticals
- Automatic cleaning program
- Electronic control and monitoring of 27 channels
- Record and data collection system for 18 channels
- cGMP compliance complete logbook for cGMP documentation
- Control via TCP/IP
- 21CFRpart11 and LIMS compatible
- Software (Windows 10, SynthraView), computer and mouse included
- Password protected user administration access to software
- Up to 10 different access levels



**Synthra MeIplus Research graphical user interface with CO and HCN option**



**Synthra MeIplus Research (standard module picture)**

## Specifications:

**[<sup>11</sup>C]Yields:** > 50 % for [<sup>11</sup>C]CH<sub>3</sub>I in less than 7 min

**Total activity is dependent on the produced [<sup>11</sup>C]CO<sub>2</sub>, which means it is dependent on the cyclotron.**

**Yields and specific activity of labeled [<sup>11</sup>C]tracers are dependent on use of proper technique and appropriate reagents.**

|   |                                   |
|---|-----------------------------------|
| Time for sequential synthesis                                       | Depends on the selected synthesis |
| Number of consecutive [ <sup>11</sup> C]CH <sub>3</sub> I syntheses | 10, then exchange of NaOH traps   |
| Dimensions  | 55 × 48 × 48 (w × d × h in cm)    |
| Weight  | Approx. 48 kg                     |
| <b>Hot Cell (minimum size)</b>                                      | 75 × 55 × 55 (w × d × h in cm)    |

## Utilities

|                           |  |
|---------------------------|--|
| Compressed air            | 4 - 8 bar<br>6 mm O.D.                         |
| Compressed He             | Purity 6.0 (99.9999 %)<br>3 - 5 bar, 1/8" O.D. |
| Compressed H <sub>2</sub> | Purity 6.0 (99.9999 %)<br>3 - 5 bar, 1/8" O.D. |
| Target gas connection     | 1/8" O.D.                                      |

## Examples for [<sup>11</sup>C]Compounds

| <b>[<sup>11</sup>C]Radiotracer</b> | <b>Target</b>                           | <b>Application</b>                                      |
|------------------------------------|---|---|
| Choline                            | Choline kinase                          | Brain tumors, prostate, lung and esophageal cancer      |
| DASB                               | SERT receptors                          | Neuropsychiatric disorders                              |
| Flumazenil                         | Benzodiazepine receptor                 | Neurodegenerative diseases                              |
| Methionine                         | Amino acid transporter                  | Brain, head and neck, lung and breast cancer, lymphomas |
| Palmitate                          | Myocardial tissue fatty acid metabolism | Heart diseases  |
| PHNO                               | D <sub>3</sub> dopamine receptors       | Neuropsychiatric disorders                              |
| Raclopride                         | D <sub>2</sub> dopamine receptors       | Neuropsychiatric disorders                              |
| Thymidine                          | Thymidine kinase-1                      | Tumor proliferation                                     |

## Warranty

I year after installation/acceptance of the equipment.