C-11 PRO2

all in one $^{11}$C radiotracer production lab
"The C-11 Pro2 has enabled our lab to synthesize an array of more than 10 different $^{11}$C compounds, with excellent day-to-day reliability and very good yields and specific activity"

Dr. Didier Le Bars
Head of PET Radiochemistry
CERMEP - Imagery Du Vivant
Bron, France

Simplify Routine Production

The C-11 Pro2 is our next generation synthesizer designed from years of R&D to simplify the routine production of $^{11}$C radiotracers. $^{11}$CO$_2$ is trapped at room temp and rapidly released using a volume optimized molecular sieve column.

Capable of producing either methyl-iodide or methyl-triflate via our highly optimised "wet" chemistry method, with labelling performed by traditional reaction vial or room temperature loop labelling*, the C-11 Pro2 also comes with built-in HPLC purification and disposable cassette S.P.E. product reformulation.

Coupled with a fully automated wash-up system, the C-11 Pro2 is the complete solution for all your $^{11}$C production requirements in the one device.

*Loop labelling method developed by A. A. Wilson et al. 2000
Synthesis Possibilities

The C-11 Pro2 easily allows the selection of the optimal synthesis route.

Step 1: Concentration of $^{11}$CO$_2$ at room temperature via molecular sieve column

Step 2: Production of $[^{11}C]$Methyl Iodide via Wet Chemistry Method in Reactor 1


Step 3B: Reactor Labelling of Precursor with Selected Synthon in Reactor 2

Step 3C: Room Temperature Loop Labelling of Precursor with Selected Synthon

Step 4: HPLC Purification

Step 5: SPE Reformulation of HPLC purified product using a disposable cassette

Step 6: Final Injectable Radiotracer

Why not have both!

Our users have discovered that along with high radiochemical yields, the C-11 Pro2 can also achieve high specific activity due to its highly optimized "wet" chemistry process.

Specific Activity

>2Ci / >74GBq / µmol at EOS
In addition to the traditional reaction vial labelling method, the C-11 Pro2 allows labelling via the room temperature loop labeling method developed by A. Wilson.

**Benefits**
- Generally less by-products are produced as the reaction is done at room temperature resulting in higher labelling yields.

**Loop Labelling**

**Reactor Labelling**

**Reactor 2** is used to preform the traditional labelling reaction method with the desired synthon.

HPLC loop is loaded with the reaction mixture using the built-in syringe drive.

**Disposable Reactors**

Two disposable 1.1mL tapered bottom glass reactors allow low volume (as low as 75uL) reactions and reduces cross-synthesis contaminants which ensures reproducible results.
The sterile disposable S.P.E. reformulation cassette and reagent set helps avoid cross-contamination and ensures reproducible results. By using non-proprietary components, the C-11 Pro2 enables users to modify and develop their own cassettes.

**Multi-Synthesis Capability**
Preform multiple radiosynthesis in one day thanks to the use of disposable components and fully automated synthesizer wash-up.

Save time and eliminate the hassle by not needing to perform manual cleaning procedures with the C-11 Pro2.

**Fully Automated Wash-Up**
Immediately post synthesis, the C-11 Pro2 preforms a fully automated wash-up procedure with 3 different solvents to clean all fixed valves and tubing.
Compact Dimensions

Install the C-11 Pro2 into virtually any hotcell

Compact Fibre Optic UV Detector
Variable wavelength and fibre optic connection to the flow cell.

Remote Flow Cell
Only the remote fibre optic flow cell is mounted inside the hotcell which frees up valuable hotcell space compared to traditional UV detectors.

Compact HPLC Pump
10 or 50mL/min pump head with integrated pressure sensor.

Compact HPLC system
The C-11 Pro2’s compact HPLC contains all the features needed to purify compounds

Width 510mm  x  Height 434mm  x  Depth 340mm
Open User Interface
System control & visual synthesis recipe development all in one platform

- Easy to use open software interface for easy tracer development
- Guides you step-by-step during the synthesis
- Can be installed on multiple computers for remote synthesis development
- Recording of all process variables and report generation (21 CFR Part 11 & GMP compliant)
- Traditional PC or Touch Screen Tablet Control
- Built-in remote diagnostics enabling simplified troubleshooting

Real-Time Sensor Trends
All sensor information can be displayed graphically in real-time trends.

Historical Data Review
Review previous synthesis results as trend graphs with data analysis functions.
Graphical **Synthesis Recipe Development**

Click • Define • Save

1. **Click a schematic**
   Click a schematic element such as solenoid valves, rotary valves & rotary actuators turn them on/off or to set positions.

2. **Define a parameter**
   Define parameters such as reactor temperatures, MFC flow, syringe/needle positions, HPLC pump parameters & step parameters (description, time, condition).

3. **Save Step**
   Click the Save Step button and the software will automatically fill-in the Excel® recipe step list automatically.

**Synthesis reports are stored as easily editable Excel® step list files.**

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**Synthesis Reports**

Generate and print synthesis reports to satisfy your labs documentation and GMP requirements.

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**Ready to Go Recipes Provided**

Each C-11 Pro2 comes with a ever growing, ready to go list of $^{11}$C radiotracer recipes.
Example of **Compounds that have been Synthesized on the C-11 Pro2**

<table>
<thead>
<tr>
<th>Radiotracer</th>
<th>Imaging</th>
<th>Avg. Yield @ E.O.S. (not corrected)</th>
<th>Synthesis time</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C-PIB</td>
<td>Beta-amyloid plaques in neuronal tissue</td>
<td>20%</td>
<td>33 mins</td>
</tr>
<tr>
<td>$^{11}$C-Choline</td>
<td>Prostate Cancer</td>
<td>48%</td>
<td>20 mins</td>
</tr>
<tr>
<td>$^{11}$C-PK11195</td>
<td>Peripheral benzodiazepine receptor (PBR)</td>
<td>10%</td>
<td>33 mins</td>
</tr>
<tr>
<td>$^{11}$C-Methionine</td>
<td>Primary brain tumors</td>
<td>40%</td>
<td>20 mins</td>
</tr>
<tr>
<td>$^{11}$C-DASB</td>
<td>Serotonin transporter</td>
<td>20%</td>
<td>33 mins</td>
</tr>
<tr>
<td>$^{11}$C-Flumazenil</td>
<td>Benzodiazepine receptor antagonist (GABA)</td>
<td>20%</td>
<td>32 mins</td>
</tr>
<tr>
<td>$^{11}$C-PE2I</td>
<td>Dopamine transporter</td>
<td>9%</td>
<td>34 mins</td>
</tr>
<tr>
<td>$^{11}$C-Acetate</td>
<td>Early metastatic prostate cancer</td>
<td>40%</td>
<td>16 mins</td>
</tr>
<tr>
<td>$^{11}$C-Raclopride</td>
<td>D2 dopamine receptors</td>
<td>10%</td>
<td>34 mins</td>
</tr>
<tr>
<td>$^{11}$C-MePPEP</td>
<td>Cannabinoid CB(1) receptor</td>
<td>10–20%</td>
<td>30 mins</td>
</tr>
<tr>
<td>$^{11}$C-SCH4427416</td>
<td>Adenosine A2 subtype receptor</td>
<td>10–20%</td>
<td>30 mins</td>
</tr>
<tr>
<td>$^{11}$C-RO154513</td>
<td>$S$ subtype – GABA - benzodiazepine receptor</td>
<td>10–20%</td>
<td>30 mins</td>
</tr>
<tr>
<td>$^{11}$C-mHED</td>
<td>Norepinephrine transporter (NET)</td>
<td>10–20%</td>
<td>30 mins</td>
</tr>
<tr>
<td>$^{11}$C-CUMI</td>
<td>5-HT(1A) agonist</td>
<td>10–20%</td>
<td>30 mins</td>
</tr>
</tbody>
</table>

Synthesis time including time required to unload $^{11}$CO$_2$ from cyclotron
iPHASE Support
Key aspects of our support structure

Technical Support
You are always a phone call or an email away from an experienced iPHASE engineer or staff member to assist with any queries. Achieving customer satisfaction is our primary objective.

Spare Parts
Complete stock of spare parts for all synthesizers are available and can be expressed shipped to you to minimise downtime.

Remote Diagnostics
Remote diagnostics are built into every system we make. This enables our experienced engineers to diagnose, test and guide the user to the quickest solution to an issue should it arise.

Continuing Education
The field of radiochemistry is ever changing and our continuing education program is there to ensure your team is fully up to date with our latest developments.

Hands on Training
Personalized hands on training will ensure your staff will easily learn and master all aspects of our automated technology.

Latest Technology
Due to the ever evolving nature of technology, we are continually applying the latest automation technologies to our systems to increase performance, productivity and reliability.
## Technical Specifications

### Hardware

<table>
<thead>
<tr>
<th>Component</th>
<th>Specifications</th>
</tr>
</thead>
</table>
| **11CO2 Trapping** | • Solid phase room temperature trapping of $^{11}$CO$_2$ onto molecular sieves  
• Rapid heating to 250°C max ($^{11}$CO$_2$ release at 180°C)  
• Compressed air cooling |
| **Reactors**       | • Dual 1.1mL disposable tapered bottom glass reactors  
• Rapid heating to 250°C max and compressed air cooling  
• Production of $^{11}$CH$_3$I in reactor 1 via the "wet" chemistry method  
• Reactor 2 used for labelling reactions with syringe driven HPLC loop loading |
| **AgOTf column**   | • Built-in with rapid heating to 250°C max for online conversion of $^{11}$CH$_3$I into $^{11}$CH$_3$OTf and compressed air cooling |
| **Labelling reaction** | • Either by traditional reaction vial (Reactor 2) or  
• Room temperature in-loop labelling* |
| **Compressed Air Cooling** | • All heater block compressed air cooling exhaust can be piped outside of the hotcell to eliminate release into the hotcell |
| **Process Valves** | • 9 chemically inert electric multi-position rotary valves  
• 13.6 bar (200 psi), 1.32 mm orifice, 20 µL internal volume |
| **HPLC Valves**    | • Built-in automatic injector  
• Manual injector (to load precursor for loop labelling reactions) with 2 mL stainless steel loop |
| **HPLC Pump**      | • Knauer HPLC pump with 10 or 50 mL/min pump head  
• Optional quaternary LPG & quad channel degasser |
| **HPLC UV Detector** | • Knauer UV/VIS detector with remote fibre optic flow cell  
• Variable wavelength (190-500 nm) |
| **Product Reformulation** | • Disposable sterile kit with reverse phase S.P.E. cartridge reformulation  
• Non-proprietary commercially available components |
| **Automation**     | • Industrial PLC with Ethernet communications to interface computer |

### Sensors

<table>
<thead>
<tr>
<th>Component</th>
<th>Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radioactivity</strong></td>
<td>6 tungsten collimated linear CsI(Tl) crystal PIN diode radioactivity detectors</td>
</tr>
<tr>
<td><strong>Pressure</strong></td>
<td>Pressure sensor for inert gas pressure monitoring</td>
</tr>
<tr>
<td><strong>Flow</strong></td>
<td>Mass Flow Controller for precise inert gas metering</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>4 x PT100 temperature sensors for reactor and column heaters</td>
</tr>
</tbody>
</table>

### Software

<table>
<thead>
<tr>
<th>Component</th>
<th>Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Graphical Interface</strong></td>
<td>Easy to use open platform operator interface with sensor trends, historical data logging &amp; analysis, synthesis reports, multi-level password protected user access, CFR 21 CFR Part 11 &amp; GMP compliant</td>
</tr>
<tr>
<td><strong>Synthesis Recipes</strong></td>
<td>Easily generated using unique Click-B-Save graphical recipe development technology and stored as Excel® step lists</td>
</tr>
<tr>
<td><strong>HPLC Control</strong></td>
<td>HPLC pump flow, eluent composition and gradients (with optional quaternary LPG pump) controlled directly from C-11 Pro2’s graphical interface</td>
</tr>
</tbody>
</table>

### Utilities and Dimensions

<table>
<thead>
<tr>
<th>Component</th>
<th>Specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compressed Air</strong></td>
<td>6-8 bar (87-116 psi), 6 mm O.D. push-in tube connection</td>
</tr>
<tr>
<td><strong>Inert Gas</strong></td>
<td>Helium, Nitrogen or Argon; 2-8 bar (29-116 psi), 1/8” O.D. tube compression connection</td>
</tr>
</tbody>
</table>
| **Case** | Compact chemically resistant powder coated case  
• Easy installation (only one electrical cable connection to PC) |
| **Dimensions** | 510 mm x 434 mm x 340 mm (WxHxD) |

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While all care has been taken to ensure that the information contained in this publication is correct, we accept no responsibility for any inaccuracy and reserve the right to modify this information. Technical specifications are based on standard operating conditions and may be subject to variations.