

C-11 PRO2

all in one ^{11}C radiotracer production lab



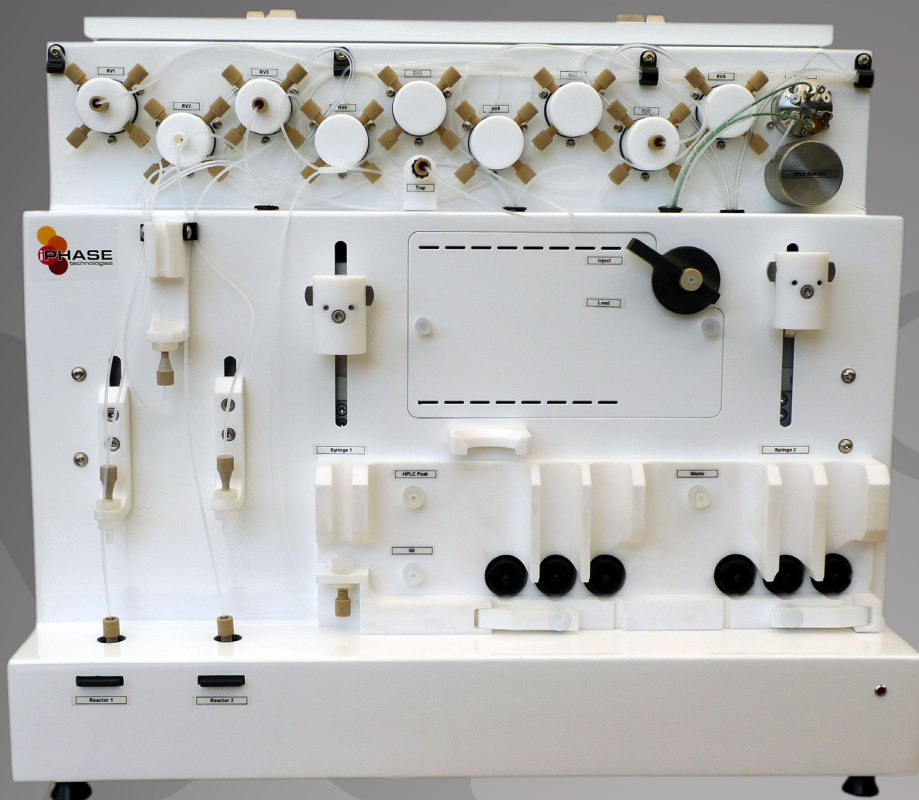
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TECHNOLOGIES

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C-11 Pro2

"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 - Imagerie 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. $^{11}\text{CO}_2$ 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.

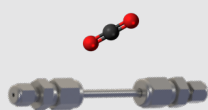
*Loop labelling method developed by A. A. Wilson et al. 2000



Synthesis Possibilities

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

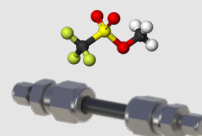
Step 1
Concentration of $^{11}\text{CO}_2$ at room temperature via molecular sieve column



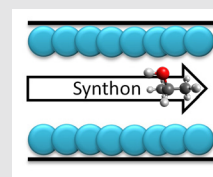
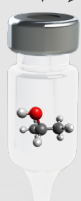
Step 2
Production of ^{11}C Methyl iodide via Wet Chemistry Method in Reactor 1



Step 3A
Online Conversion of ^{11}C Methyl iodide into ^{11}C Methyl Triflate

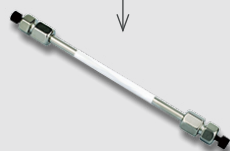


Step 3B
Reactor Labelling of Precursor with Selected Synthon in Reactor 2

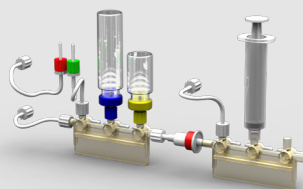


Step 3C:
Room Temperature Loop Labelling of Precursor with Selected Synthon

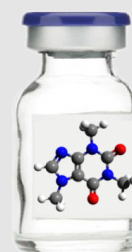
Step 4
HPLC Purification



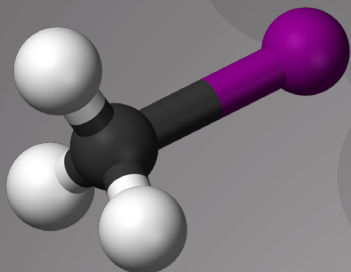
Step 5
SPE Reformulation of HPLC purified product using a disposable cassette



Step 6
Final Injectable Radiotracer

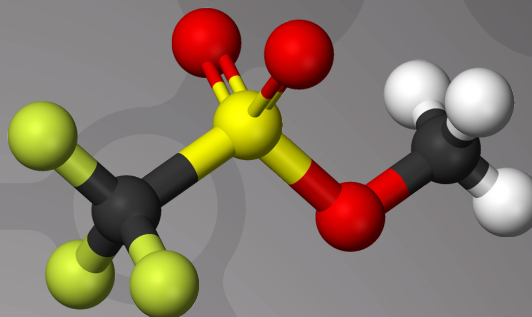


$[^{11}\text{C}]$ Methyl-Iodide & $[^{11}\text{C}]$ Methyl-Triflate



$[^{11}\text{C}]$ Methyl-Iodide

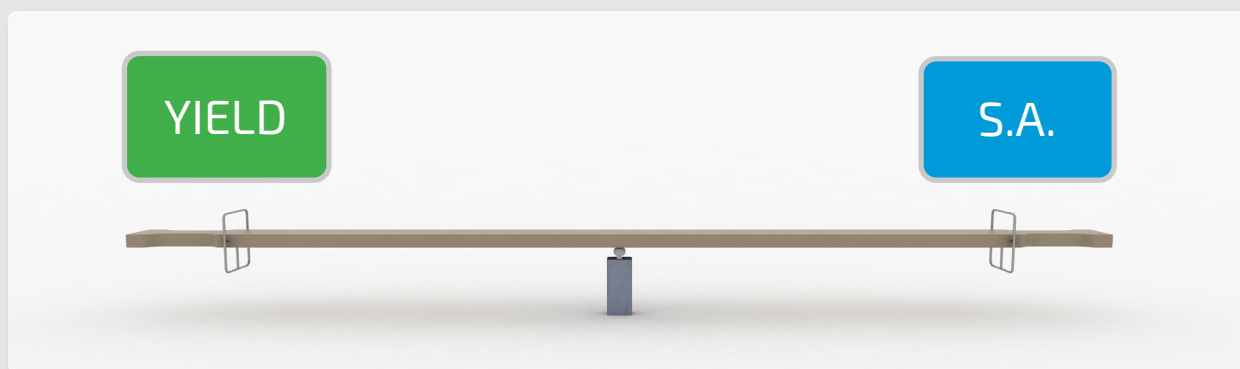
$[^{11}\text{C}]$ Methyl Iodide is produced in Reactor 1 via the "wet chemistry" method and it achieves a $> 85\%$ conversion rate from $[^{11}\text{C}]$ carbon dioxide to $[^{11}\text{C}]$ methyl-iodide.



$[^{11}\text{C}]$ Methyl-Triflate

The built-in silver triflate column allows on-line rapid conversion of $[^{11}\text{C}]$ methyl-iodide into $[^{11}\text{C}]$ methyl-triflate.

Yields & Specific Activity



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

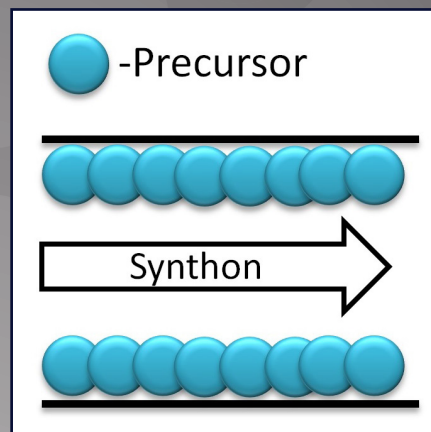
3-5Ci / 111-185GBq / μmol at EOS

Loop Labelling

In addition to the traditional reaction vial labelling method, the C-11 Pro2 allows labelling via the room temperature loop labelling 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.



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.

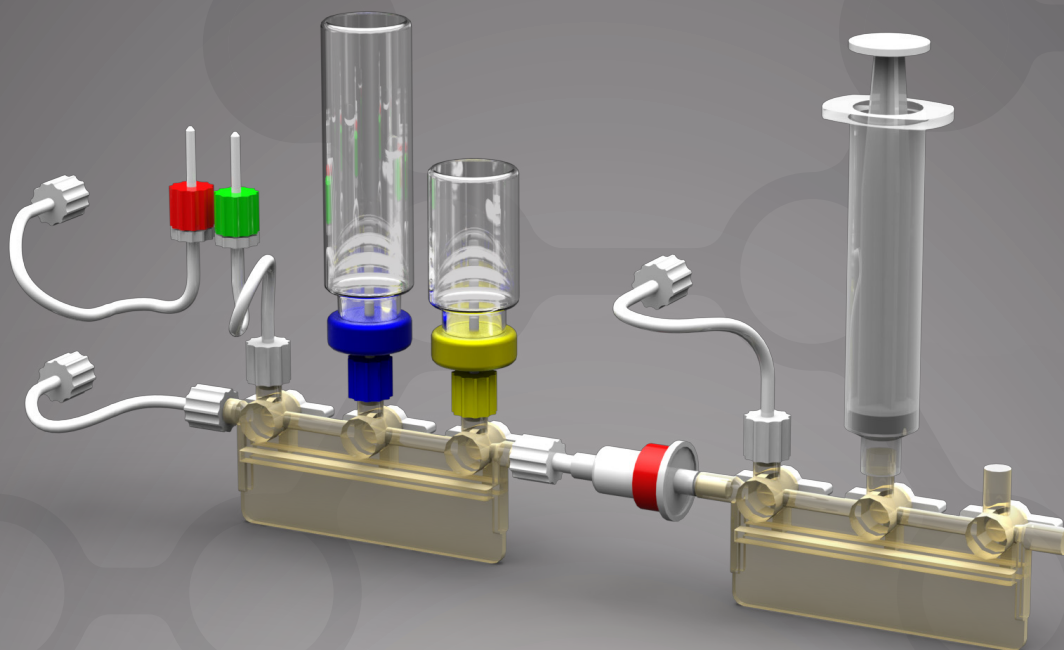


Reactor 1

Reactor 2

Disposable SPE Reformulation Cassette

Simplify GMP requirements



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

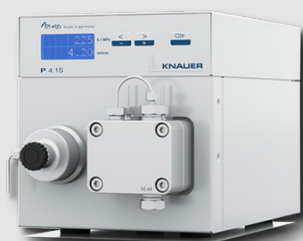
Install the C-11 Pro2 into virtually any hotcell



Width 51cm x Height 43.4cm x Depth 34cm

Compact HPLC system

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



Compact HPLC Pump

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



Compact Fibre Optic

UV Detector

Variable wavelength and fibre
optic connection to the flow
cell.

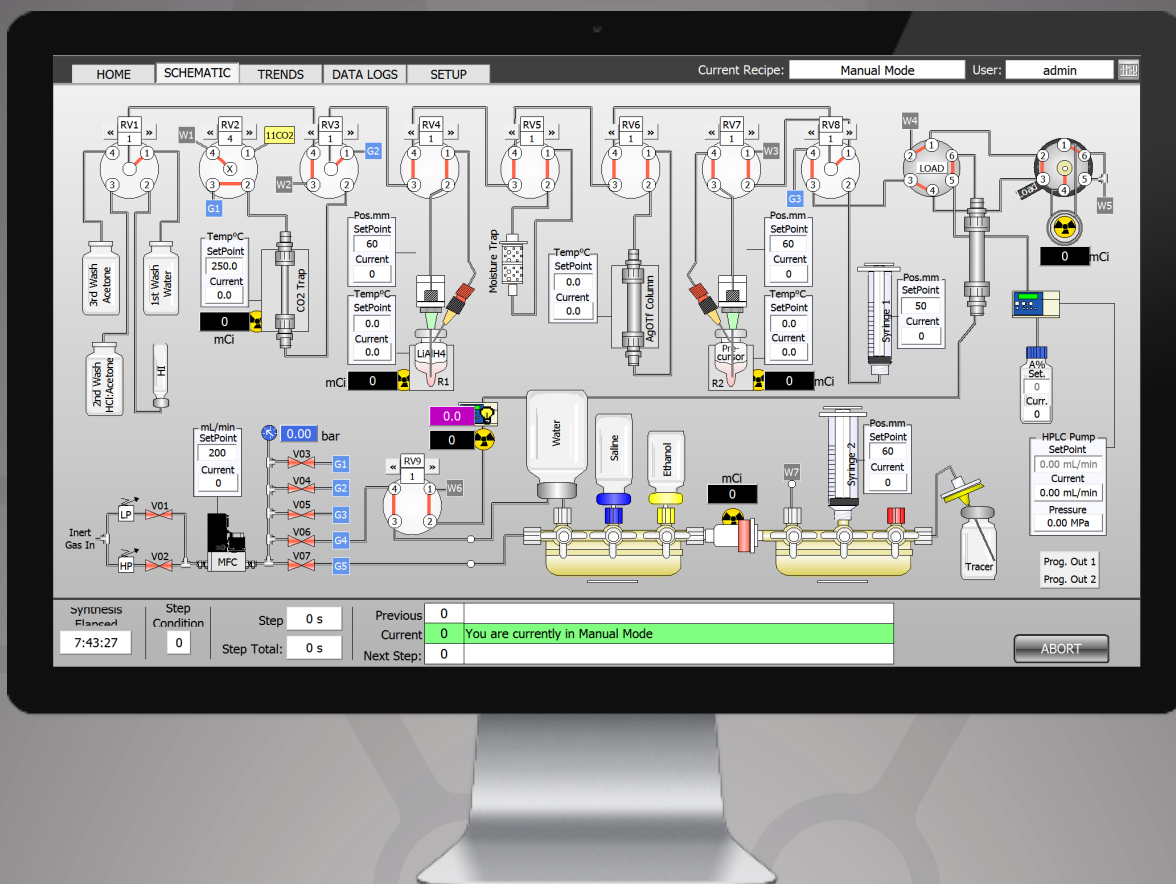


Remote Flow Cell

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

Open User Interface

System control & visual synthesis recipe development
all in one platform



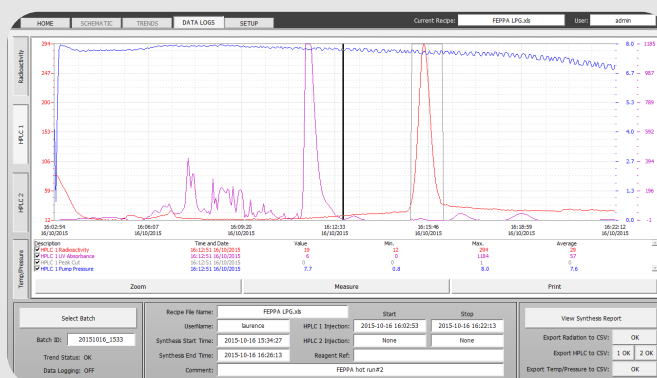
- ✓ Easy to use open software interface for easy tracer development
- ✓ Guides you step-by-step during the synthesis
- ✓ Can be installed on multiple computers for remote synthesis development

- ✓ 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.

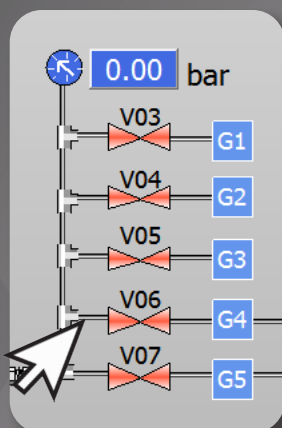


Historical Data Review

Review previous synthesis results as trend graphs with data analysis functions.

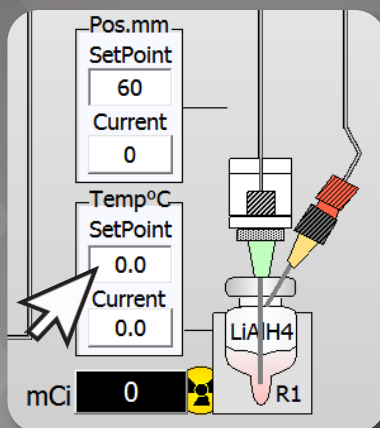
Graphical **Synthesis Recipe** Development

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).

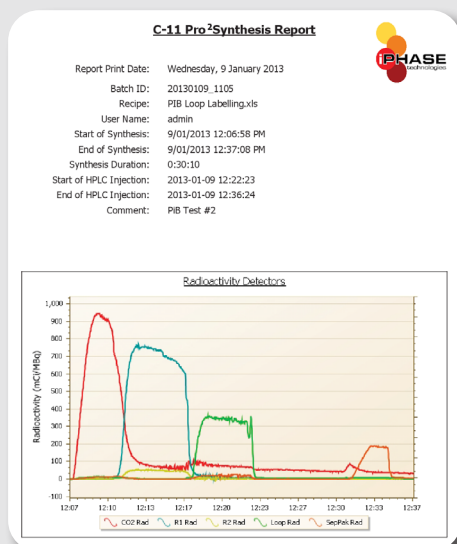


3. Save Step

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

Step	Step Message	Step Condition	Step Time Seconds	Rotary Valve Position					HPLCV1 Valve	Manifold Rotary Tap Position (0=off, 1=on)			Gas Valve Status (0=off, 1=on)			Temp °C (0-255)				Needle Position (0-60mm)		Syringe Position (0-50mm)		HPLC Pump Flow (0.0-50.0)	HPLC Eluent (0-100%)			
				(1-4) RV1	(1-4) RV2	(1-4) RV3	(1-2) RV4	(1-2) RV5		RT1	RT2	RT3	V1	V2	V3	CO2 Trap	Reactor 1	Reactor 2	AgOTf Column	Reactor 1	Reactor 2	Syringe 1	Syringe 2		A%	B%	C%	D%
71	Synthesizer ready - Press NEXT when ready to transfer target activity	0	0	1	2	1	1	1	0	0	0	0	0	0	0	30	0	0	220	18	18	33	0	5.0	100	0	0	0
72	Transfer target activity now - Press NEXT when transfer complete	1	0	1	3	4	1	1	0	0	0	0	0	0	0	30	0	0	220	18	18	33	0	5.0	100	0	0	0
73	Heating CO2 Trap - Heat-up phase	10	400	1	4	4	1	1	0	0	0	0	1	1	1	150	0	0	220	18	18	33	0	5.0	100	0	0	0
74	Heating CO2 Trap - Setpoint heating	0	10	1	4	4	1	1	0	0	0	0	1	1	1	190	0	0	220	18	18	33	0	5.0	100	0	0	0
75	Lowering Reactor 1 needle into LiAlH4	40	5	1	4	2	2	1	0	0	0	0	1	1	1	190	0	0	220	0	18	33	0	5.0	100	0	0	0
76	Trapping C-11 in Reactor 1 - Waiting for Maximum Activity!	31	180	1	4	2	2	1	0	0	0	0	1	1	1	190	0	0	220	0	18	33	0	5.0	100	0	0	0
77	Evaporating THF - Heat-up phase	11	120	1	4	2	2	1	0	0	0	0	1	1	1	190	85	0	220	0	18	33	0	5.0	100	0	0	0
78	Evaporating THF - Setpoint heating low flow	0	45	1	4	2	2	1	0	0	0	0	1	1	1	0	85	0	220	0	18	33	0	5.0	100	0	0	0
79	Evaporating THF - Setpoint heating higher flow	0	15	1	4	2	2	1	0	0	0	0	1	1	1	0	85	0	220	0	18	33	0	5.0	100	0	0	0

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




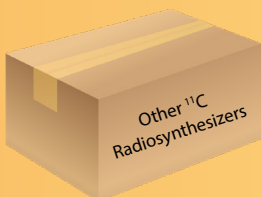
Synthesis Reports

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



Ready to Go Recipes Provided
 Each C-11 Pro2 comes with a ever growing, ready to go list of ¹¹C radiotracer recipes.

Feature Comparison

Feature		
[¹¹ C]Methly-Iodide Yield	>85%	50%
[¹¹ C]Methly -Triflate Column Built-in	✓	✓*
Reactor Labelling	✓	✓
Loop Labelling	✓	
Disposable S.P.E. Cassette	✓	
Variable Wavelength Fibre Optic UV/VIS Detector	✓	✓
Visual Synthesis Recipe Development	✓	

* Optional Feature

Example of Compounds that have been Synthesized on the C-11 Pro2

Radiotracer	Imaging	Avg. Yield @ E.O.S. (not corrected)	Synthesis time
¹¹ C-PIB	Beta-amyloid plaques in neuronal tissue	20%	33 mins
¹¹ C-Choline	Prostate Cancer	48%	20 mins
¹¹ C-PK11195	Peripheral benzodiazepine receptor (PBR)	10%	33 mins
¹¹ C-Methionine	Primary brain tumors	40%	20 mins
¹¹ C-DASB	Serotonin transporter	20%	33 mins
¹¹ C-Flumazenil	Benzodiazepine receptor antagonist (GABA)	20%	32 mins
¹¹ C-PE2I	Dopamine transporter	9%	34 mins
¹¹ C-Acetate	Early metastatic prostate cancer	40%	16 mins
¹¹ C-Raclopride	D2 dopamine receptors	10%	34 mins
¹¹ C-MePPEP	Cannabinoid CB(1) receptor	10-20%	30 mins
¹¹ C-SCH442,416	Adenosine A2 subtype receptor	10-20%	30 mins
¹¹ C-RO154513	5 subtype - GABA - benzodiazepine receptor	10-20%	30 mins
¹¹ C-mHED	Norepinephrine transporter (NET)	10-20%	30 mins
¹¹ C-CUMI	5-HT(1A) agonist	10-20%	30 mins

Synthesis time including time required to unload ¹¹CO₂ from cyclotron

iPHASE Support

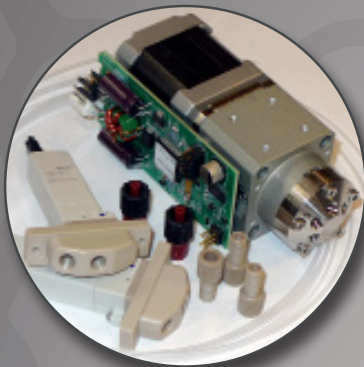
Key aspects of our support structure

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.

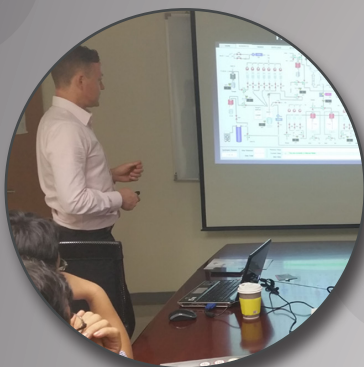


Remote Diagnostics

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.



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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.



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.



Hands on Training

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

Technical Specifications

Hardware	
¹¹ CO ₂ Trapping	<ul style="list-style-type: none"> • Solid phase room temperature trapping of ¹¹CO₂ onto molecular sieves • Rapid heating to 250°C max (¹¹CO₂ release at 180°C) • Compressed air cooling
Reactors	<ul style="list-style-type: none"> • Dual 1.1 mL disposable tapered bottom glass reactors • Rapid heating to 250°C max and compressed air cooling • Production of ¹¹CH₃I in reactor 1 via the "wet" chemistry method • Reactor 2 used for labelling reactions with syringe driven HPLC loop loading
AgOTf column	<ul style="list-style-type: none"> • Built-in with rapid heating to 250°C max for online conversion of ¹¹CH₃I into ¹¹CH₃OTf and compressed air cooling
Labelling reaction	<ul style="list-style-type: none"> • Either by traditional reaction vial (Reactor 2) or • Room temperature in-loop labelling*
Compressed Air Cooling	<ul style="list-style-type: none"> • All heater block compressed air cooling exhaust can be piped outside of the hotcell to eliminate release into the hotcell
Process Valves	<ul style="list-style-type: none"> • 9 chemically inert electric multi-position rotary valves • 13.6 bar (200 psi), 1.32 mm orifice, 20 µL internal volume
HPLC Valves	<ul style="list-style-type: none"> • Built-in automatic injector • Manual injector (to load precursor for loop labelling reactions) with 2 mL stainless steel loop
HPLC Pump	<ul style="list-style-type: none"> • Knauer HPLC pump with 10 or 50 mL/min pump head • Optional quaternary L.P.G. & quad channel degasser
HPLC UV Detector	<ul style="list-style-type: none"> • Knauer UV/VIS detector with remote fibre optic flow cell • Variable wavelength (190-500 nm)
Product Reformulation	<ul style="list-style-type: none"> • Disposable sterile kit with reverse phase S.P.E. cartridge reformulation • Non-proprietary commercially available components
Automation	<ul style="list-style-type: none"> • Industrial PLC with Ethernet communications to interface computer

Sensors	
Radioactivity	<ul style="list-style-type: none"> • 6 tungsten collimated linear CsI(Tl) crystal PIN diode radioactivity detectors
Pressure	<ul style="list-style-type: none"> • Pressure sensor for inert gas pressure monitoring
Flow	<ul style="list-style-type: none"> • Mass Flow Controller for precise inert gas metering
Temperature	<ul style="list-style-type: none"> • 4 x PT100 temperature sensors for reactor and column heaters

Software	
Graphical Interface	<ul style="list-style-type: none"> • Easy to use open platform operator interface with sensor trends, historical data logging & analysis, synthesis reports, multi-level password protected user access, CFR 21 CFR Part 11 & GMP compliant
Synthesis Recipes	<ul style="list-style-type: none"> • Easily generated using unique Click-&-Save graphical recipe development technology and stored as Excel® step lists
HPLC Control	<ul style="list-style-type: none"> • HPLC pump flow, eluent composition and gradients (with optional quaternary LPG pump) controlled directly from C-11 Pro2's graphical interface

Utilities and Dimensions	
Compressed Air	<ul style="list-style-type: none"> • 6-8 bar (87-116 psi), 6 mm O.D. push-in tube connection
Inert Gas	<ul style="list-style-type: none"> • Helium, Nitrogen or Argon; 2-8 bar (29-116 psi), 1/8" O.D. tube compression connection
Case	<ul style="list-style-type: none"> • Compact chemically resistant powder coated case • Easy installation (only one electrical cable connection to PC)
Dimensions	<ul style="list-style-type: none"> • 510 mm x 434 mm x 340 mm (WxHxD)

