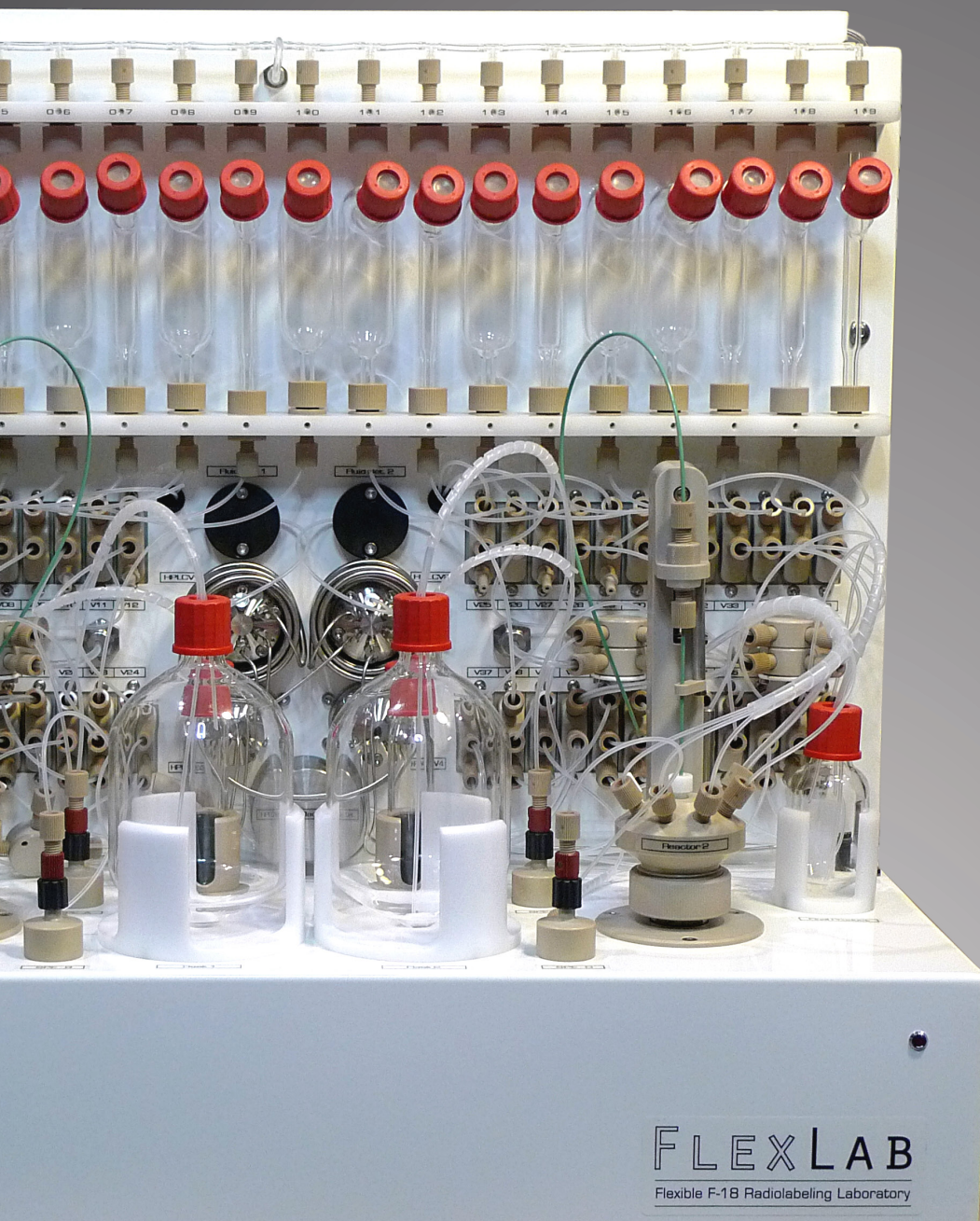


FLEXLAB

multi-step ^{18}F radiotracer production lab



www.iphase.com.au



FlexLab

*"For complex multi step
 ^{18}F radiotracer research &
development, the FlexLab has
been invaluable"*

Dr. Uwe Ackermann
Chief Research Radiochemist
Austin Hospital
Melbourne, Australia



Multi-Step ^{18}F Radiotracer Development & Production Platform

The FlexLab is the most versatile ^{18}F radiosynthesizer specifically suited to the research, development and fully automated production of multi-step radiotracers.

The FlexLab allows the radiochemist to fully automate the radiosynthesis of multi-step compounds thereby improving synthesis yields, simplifying daily production and most importantly reducing the operators radiation exposure by completely eliminating the need to perform any manual processes.

Synthesis Possibilities

The FlexLab is the only radiosynthesizer that is able to fully automate all the following synthesis steps:

Step 1

^{18}F Trapping onto QMA cartridge

Step 2



Reactor 1 Primary labelling

Step 3



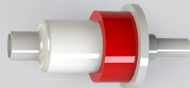
SPE Purification of Primary Reaction Mixture

Step 4



HPLC purification of Primary Reaction Mixture

Step 5



SPE Reformulation of Primary HPLC product

Step 6



Reactor 2 Secondary Reaction

Step 7



SPE Purification of Secondary Reaction Mixture

Step 8

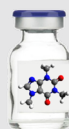


HPLC Purification of Secondary Reaction Mixture

Step 9



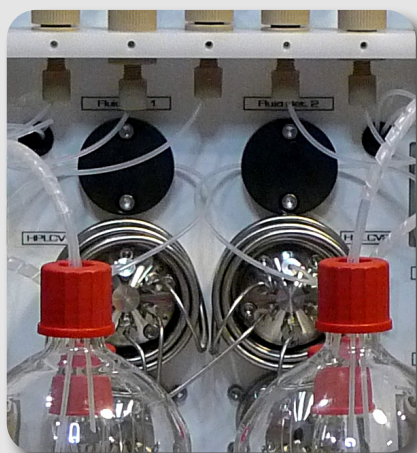
SPE Reformulation of Secondary HPLC product



Final Injectable Radiotracer

HPLC **Without** Limitations

The FlexLab's HPLC system has been designed to give the radiochemist all the tools they need to purify complex multi-step compounds without any compromises.



Dual HPLC Injectors

Allows two independent HPLC purifications in the one synthesis using independent HPLC valves, HPLC loops & HPLC columns.



Dual HPLC Product SPE Reformulation

Perform two independent S.P.E. purification of the collected HPLC product (one per HPLC system).



Dual HPLC Column Selector

Automatically select between two different HPLC columns with also a column by-pass setting for cleaning.



4 x HPLC Eluents

Automatic selection between the 4 eluents.

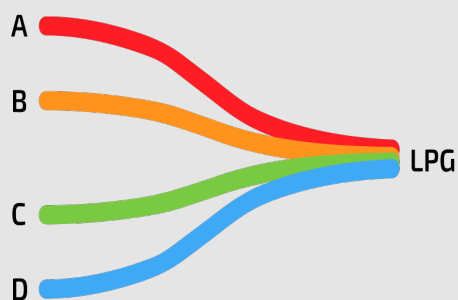
Fiber Optic UV/VIS Detector

Variable wavelength with a remote fiber optic flow cell.

Quaternary Low Pressure Gradient HPLC Pump

10mL/min (option 50mL/min) pump head, quad channel degasser and mixer built-in.

HPLC equipment images: KNAUER Wissenschaftliche Geräte GmbH



HPLC Low Pressure Gradients

Easily perform fully automated quaternary L.P.G. solvent elutions during your radiosynthesis. All parameters are defined in your recipe file.

Eliminate Manual Solvent Mixing

Quaternary L.P.G. eliminates the need for manual mixing of your HPLC eluent - It's all done on-line.

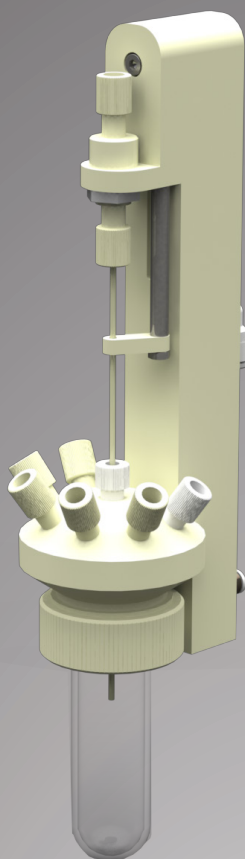
Fiber Optic UV Flow Cell

Only the remote fiber optic flow cell is mounted inside the hotcell which frees up valuable space compared to a standard UV detector.

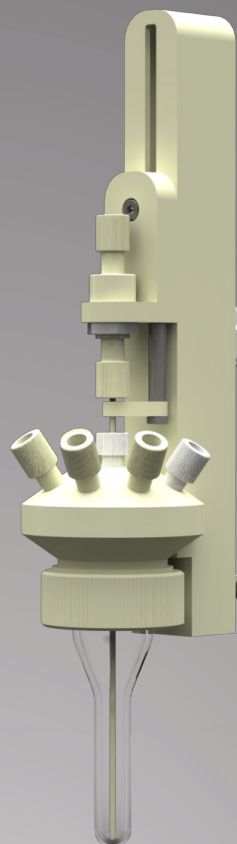
Flexible Reactors

Easily swap between the standard 20mL reactor and the small volume 2mL reactor

Reactors available in either standard borosilicate glass or high purity glassy carbon. Heating to 220°C & vortex tube compressed air cooling to $\approx 8^{\circ}\text{C}$.



Standard
20mL reactor



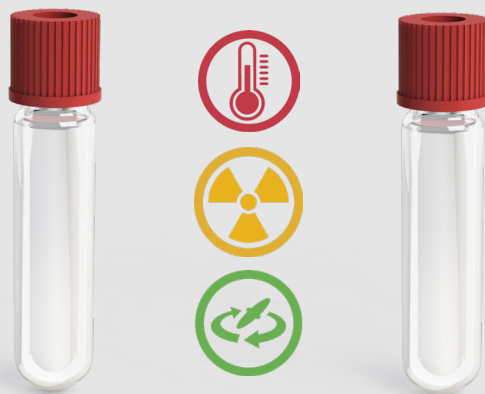
Small volume
2mL reactor

Open up new possibilities with the quick change small volume reactors by simplifying the transition to peptide radiolabelling.



LN₂ Main Reactor Cooling

Extend the cooling range of both main reactors to -80°C by combining it with our dual reactor LN₂ cooling option.



Quad Reactors

Add unparalleled quad reactor capabilities to the FlexLab. The quad reactor option adds heating to 150°C / cooling to ambient, radioactivity monitoring and magnetic stirrer bar mixing to both intermediate vials.

Compact Dimensions

Install the FlexLab into virtually any hotcell

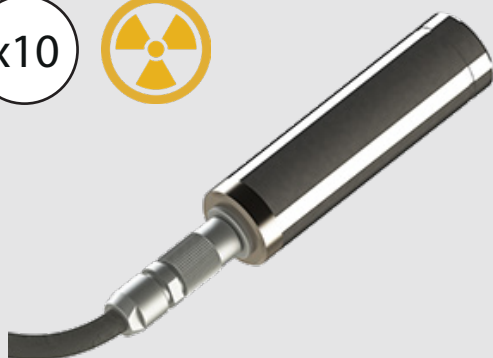


FlexLab dimensions Width 49.4cm x Height 46.6cm x Depth 41.6cm

Reduce your labs hotcell costs. No longer do you need a large and expensive research hotcell to house all the equipment needed for complex multi-step synthesis.

The FlexLab easily fits into compact hotcell's with internal dimensions as small as 72cm x 60cm x 60cm (WxHxD) which can substantially reduce your laboratories costs.

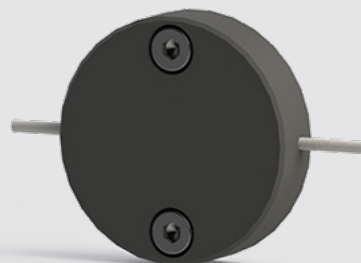
x10



Radioactivity Detectors

Monitor every step of the synthesis with 10 collimated radioactivity detectors. CsI(Tl) crystal PIN photodiodes provide a linear response across a large radioactivity range.

* 12 with quad reactor option

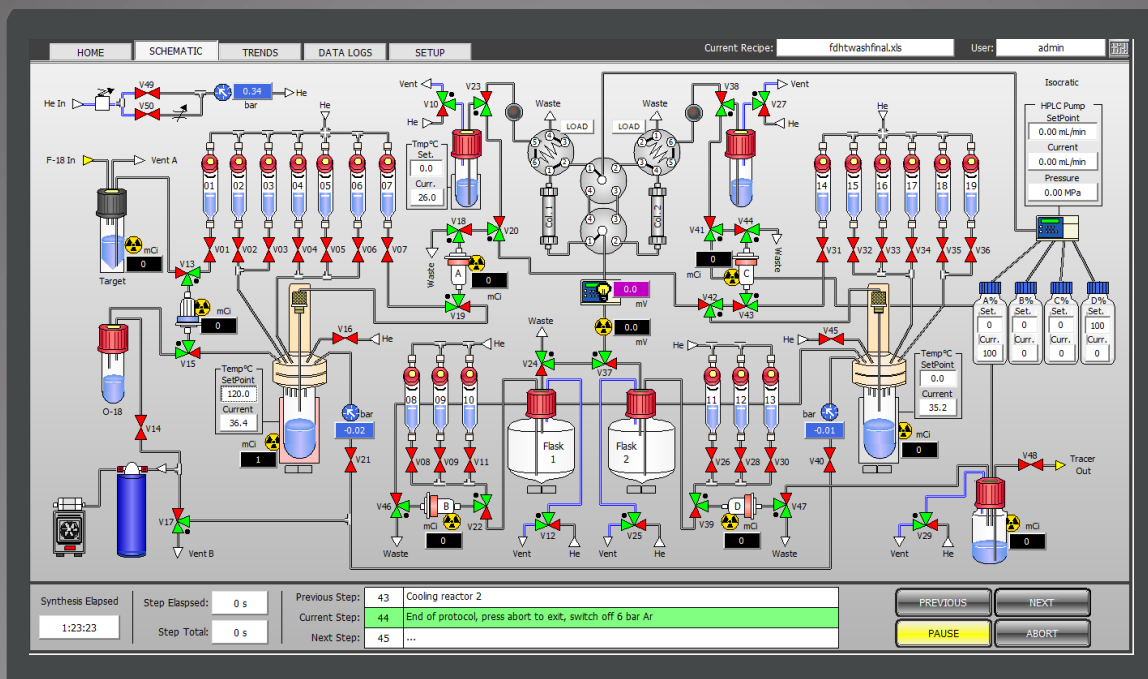


HPLC Injection Fluid Detectors

Product injection into the HPLC loop's is controlled by two software calibrated optical fluid detectors. They allow on the fly adjustment of the detection threshold so that you never miss your product injection.

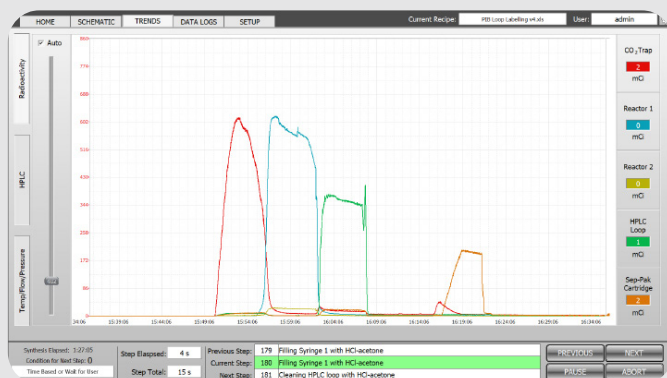
Open User Interface

System control & visual synthesis recipe development all in one platform



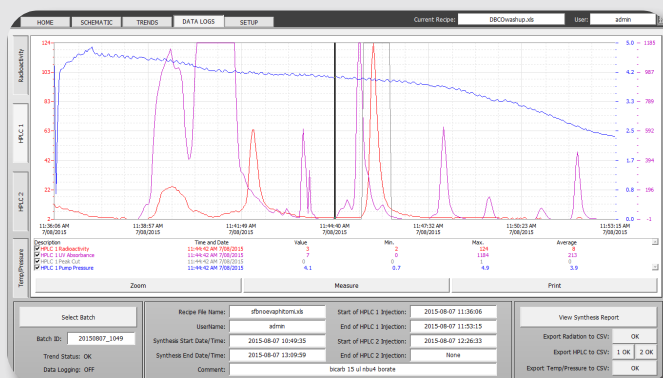
- ✓ Easy to use open software interface for easy tracer development
- ✓ Guides you step-by-step during the synthesis
- ✓ Can be installed on multiple computers for remote synthesis development

- ✓ 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.

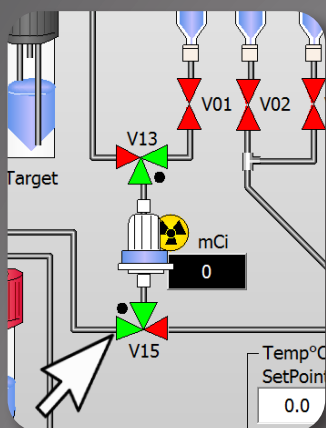


Historical Data Review

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

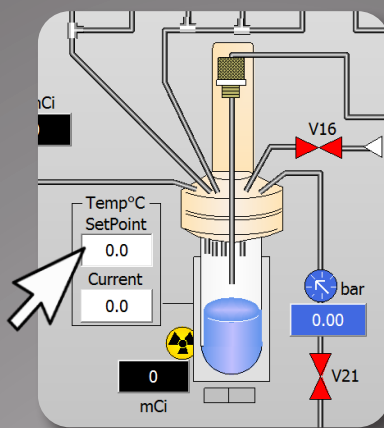
Graphical **Synthesis Recipe** Development

Click • Define • Save



1. Click a schematic

Click a schematic element such as valves, magnetic stirrers & vacuum pump to turn them on/off.



2. Define a parameter

Define parameters such as reactor temperatures, HPLC pump parameters (flow rate & eluent composition) & step parameters (description, time, condition).

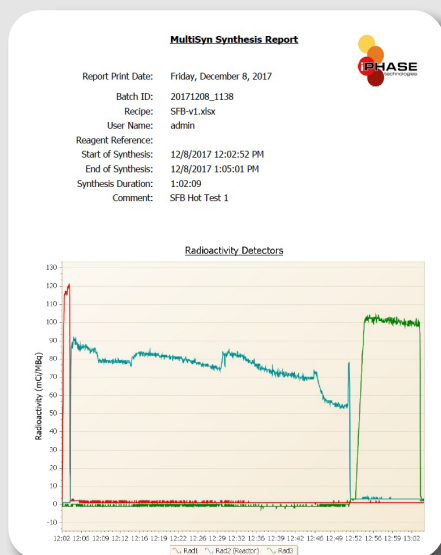


3. Save Step

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

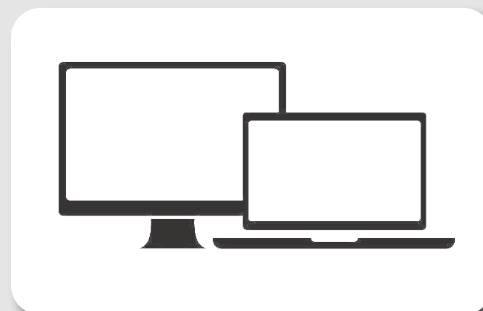
| | | | 0=off, 1=on | | | | 0=inject, 1=load | | Temp °C 0-255 | | 0=up, 1=down | | 0=off, 1=on | | 0=off, 1=on |
|---|----------------|-------------------|-------------|-----|-----|-----|------------------|---------|---------------|-----------|----------------|----------------|-------------------|-------------------|-------------|
| Step Message | Step Condition | Step Time Seconds | V01 | V02 | V03 | V04 | HPLC V1 | HPLC V2 | Reactor 1 | Reactor 2 | Reactor 1 Tube | Reactor 2 Tube | Reactor 1 Stirrer | Reactor 2 Stirrer | Vacuum Pump |
| Ready for F- from cyclotron | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Trapping F- onto QMA | 0 | 60 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| Elution of QMA to Reactor 1 | 0 | 45 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| Evaporation to dryness | 0 | 600 | 0 | 0 | 1 | 0 | 0 | 0 | 90 | 0 | 0 | 1 | 1 | 0 | 1 |
| Cooling reactor 1 | 12 | 600 | 0 | 0 | 0 | 0 | 0 | 1 | 50 | 160 | 0 | 0 | 1 | 1 | 1 |
| Addition of precursor (vial 3) to reactor 1 | 0 | 30 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 120 | 1 | 0 | 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.



Install on Multiple Computers

Develop the synthesis recipe in your office and test the recipe in the lab.

Feature Comparison

| Feature |  |  |
|---|--|---|
| Dual Reactors | ✓ | ✓ |
| Quad Reactors | ✓ * | |
| LN ₂ Reactor Cooling | ✓ * | ✓ |
| Dual Independent HPLC Purification | ✓ | |
| Dual S.P.E. HPLC Product Reformulation | ✓ | |
| Quaternary LPG Pump with Degasser | ✓ | ✓ * |
| Variable Wavelength Fiber Optic UV/VIS Detector | ✓ | |
| Visual Synthesis Recipe Development | ✓ | |

* Optional feature

Example of Tracers that have been Synthesized On The FlexLab

| Radiotracer | Imaging | Avg. Yield @ E.O.S. (not corrected) | Reference |
|---|--|-------------------------------------|--------------------------|
| ¹⁸ F-FLT | Proliferation | ~10% | Ackermann |
| ¹⁸ F-FLETT (synthon: ¹⁸ F-FEA) | Proliferation | ~40% | Ackermann |
| ¹⁸ F-FMISO | Hypoxia | ~30% | Ackermann |
| ¹⁸ F-NaphtoQuinone (synthon: ¹⁸ F-FB) | Hypoxia | ~10% | Ackermann |
| ¹⁸ F-FES | Estrogen | ~20% | Ackermann |
| ¹⁸ F-MEL50/54 | Melanoma | | ANSTO |
| ¹⁸ F-FDHT | Tumour: Androgen receptor expression | ~20% | Ackermann |
| ¹⁸ F-FPPRGD ₂ (synthon: ¹⁸ F-NFP) | Peptide (α & β ₃ integrin expression) | ~10% | Roselt |
| ¹⁸ F-GalactoRGD (synthon: ¹⁸ F-NFP) | Peptide (α & β ₃ integrin expression) | ~10% | Roselt |
| ¹⁸ F-PBR111 | Peripheral Benzodiazepine Receptor | ~30% | Bourdier |
| Synthons | | | |
| ¹⁸ F-SFB: N-Succinimidyl 4-[¹⁸ F]Fluorobenzoate | Antibody: coupling to free amine of single chain antibody | ~25% | Roselt, Ackermann, ANSTO |
| ¹⁸ F-FEA: 2-[¹⁸ F]Fluoroethylazide | Peptide (Cu catalysed click chemistry) | ~90% | Ackermann |
| ¹⁸ F-FP: 2-[¹⁸ F]Fluoropropionic acid | Peptide | ~20% | Roselt |
| ¹⁸ F-NFP: 4-nitrophenyl 2-[¹⁸ F]fluoropropionate | Neovascularisation: coupling to peptide | ~20% | Roselt |
| ¹⁸ F-FB: [¹⁸ F]Fluorobenzoic acid | Coupling to hydroxymethyl naphthoquinone | ~35% | Ackermann |
| ¹⁸ F-FBEM: N-[2-(4-[¹⁸ F]Fluorobenzamido)Ethyl] maleimide | Coupling to sulfhydryl group of modified single chain antibody | ~25% | Ackermann |
| ¹⁸ F-FBA: 4-[¹⁸ F]Fluorobenzaldehyde | Coupling to amine | ~40% | Ackermann, Roselt |
| ¹⁸ F-DBCO: [¹⁸ F]-Dibenzocyclooctyne (free amine on chain) | Peptide: Cu-free click chemistry | ~10% | Ackermann |

End of Synthesis radiochemical yield not decay corrected.

iPHASE Support

Key aspects of our support structure

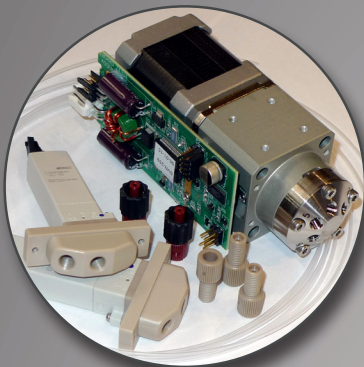
Technical Support

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.



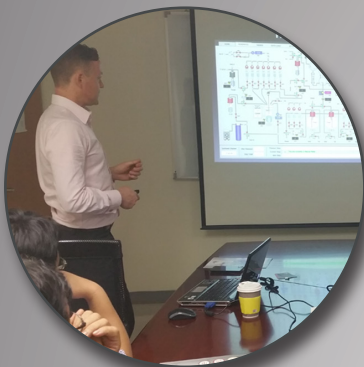
Spare Parts

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.



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 | |
|--------------------------|---|
| Reactors | <ul style="list-style-type: none"> • Dual 20 mL glass reactors with magnetic stirrers • Quick-change 2 mL small volume reactor for low volume reagent reactions • Heating to 220°C and built-in Vortex tube compressed air cooling to approx. 8°C • 2-position PEEK tube with full extension to top of reactor for efficient distillations |
| Reagent Vials | <ul style="list-style-type: none"> • 19 glass reagent storage vials: 1 mL, 3 mL & 15 mL volumes |
| Process Valves | <ul style="list-style-type: none"> • 50 chemically inert PEEK solenoid valves • Kalrez® seals, 2.5 bar, 1.4 mm orifice, 20 µL dead volume |
| Reaction Purification | <ul style="list-style-type: none"> • Reverse and normal phase S.P.E. cartridge purification and/or HPLC purification of reaction intermediates for both reactors |
| HPLC Valves | <ul style="list-style-type: none"> • Dual independent HPLC injectors with 5 mL loops (different volume loops can be installed) • Dual HPLC column selector with column bypass feature for HPLC system cleaning |
| HPLC Pump | <ul style="list-style-type: none"> • Knauer HPLC pump with 10 or 50 mL/min pump head • Quaternary Low Pressure Gradient (LPG) controller • Quad channel degasser |
| HPLC UV Detector | <ul style="list-style-type: none"> • Knauer UV/VIS detector with remote fibre optic flow cell • Variable wavelength (190-750 nm) |
| Product Reformulation | <ul style="list-style-type: none"> • Dual reverse phase S.P.E. cartridge reformulation systems |
| Automation | <ul style="list-style-type: none"> • Industrial PLC with Ethernet communications to interface computer |
| Options | <ul style="list-style-type: none"> • Liquid nitrogen cooling of main reactors to -80°C • Quad reactors enabling heating to 150°C, compressed air cooling to ambient, magnetic stirring and radioactivity monitoring of both intermediate vials • Drop-in intermediate vial heater insert with heating to 100°C add's essentially a third reactor (for FlexLab's not fitted with quad reactor option) <div>   </div> |
| Sensors | |
| Radioactivity | <ul style="list-style-type: none"> • 10 tungsten collimated linear CsI(Tl) crystal PIN diode radioactivity detectors. 12 with quad reactor option |
| Pressure | <ul style="list-style-type: none"> • 3 pressure sensors for reactor and inert gas pressure monitoring |
| Temperature | <ul style="list-style-type: none"> • PT100 temperature sensors for reactor temperatures |
| Fluid | <ul style="list-style-type: none"> • Dual software calibrated optical fluid detectors for reliable HPLC loop loading |
| 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 low pressure gradients controlled directly from FlexLab's graphical user interface |
| Utilities and Dimensions | |
| Compressed Air | <ul style="list-style-type: none"> • 6-8 bar (87-116 psi), 1/4" 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"> • 494 mm x 466 mm x 416 mm (WxHxD) |

