

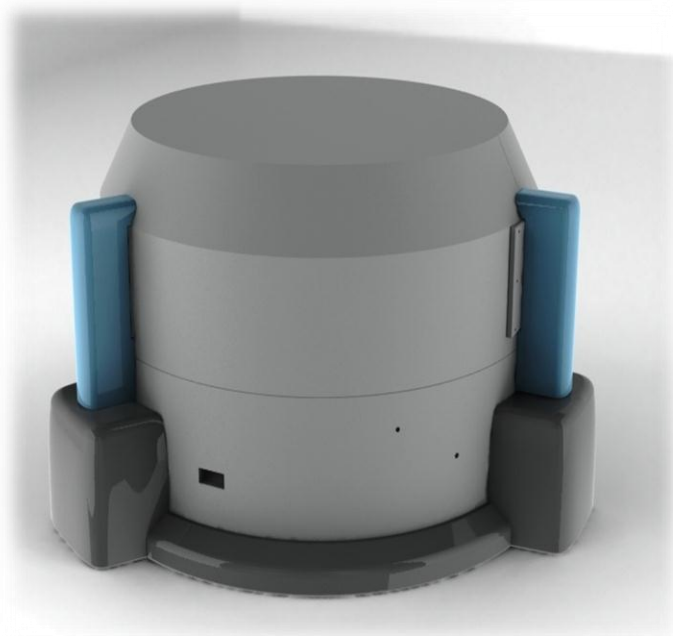


ABT Molecular Imaging, Inc.

“Dose-on-Demand”
Biomarker Generator System
for Molecular Imaging

The Principle

A single operator producing individual patient doses that have been verified by automated quality control, with a system that can fit next to the PET/CT



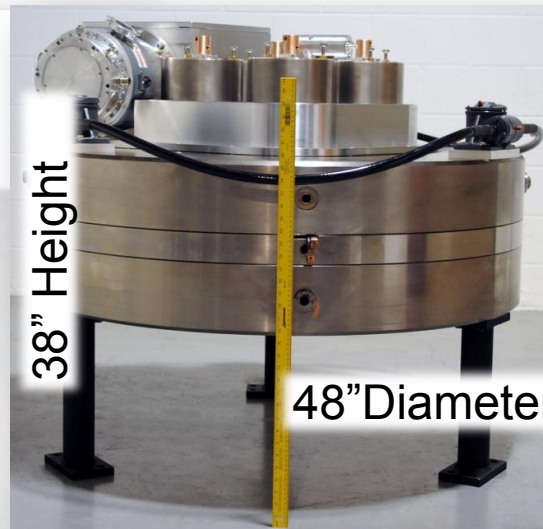
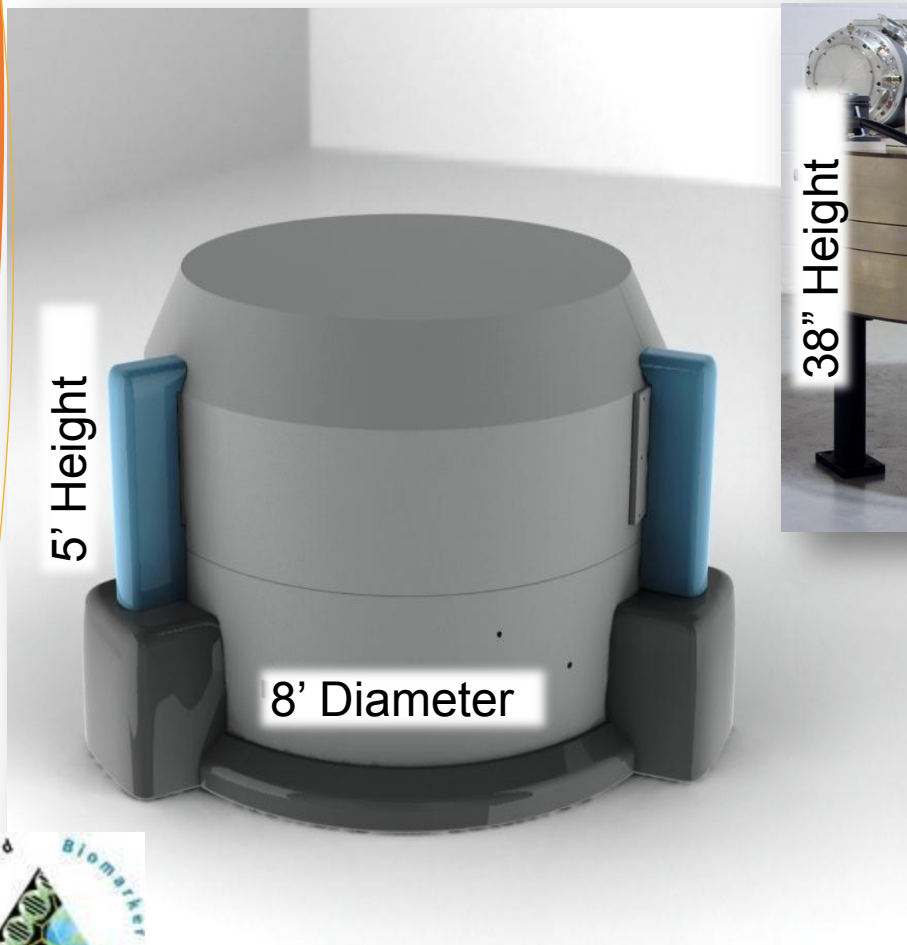
Company History

ABT has many years of experience in cyclotron, chemistry, and medical equipment design. The company founder, Dr. Ron Nutt, and his engineering team, developed technology at CTI Molecular Imaging. CTI was purchased by Siemens in 2006, the year ABT Molecular Imaging was formed.



The Biomarker Generator System

Accelerator with Self-Shielding , Microchemistry and Integrated Quality Control

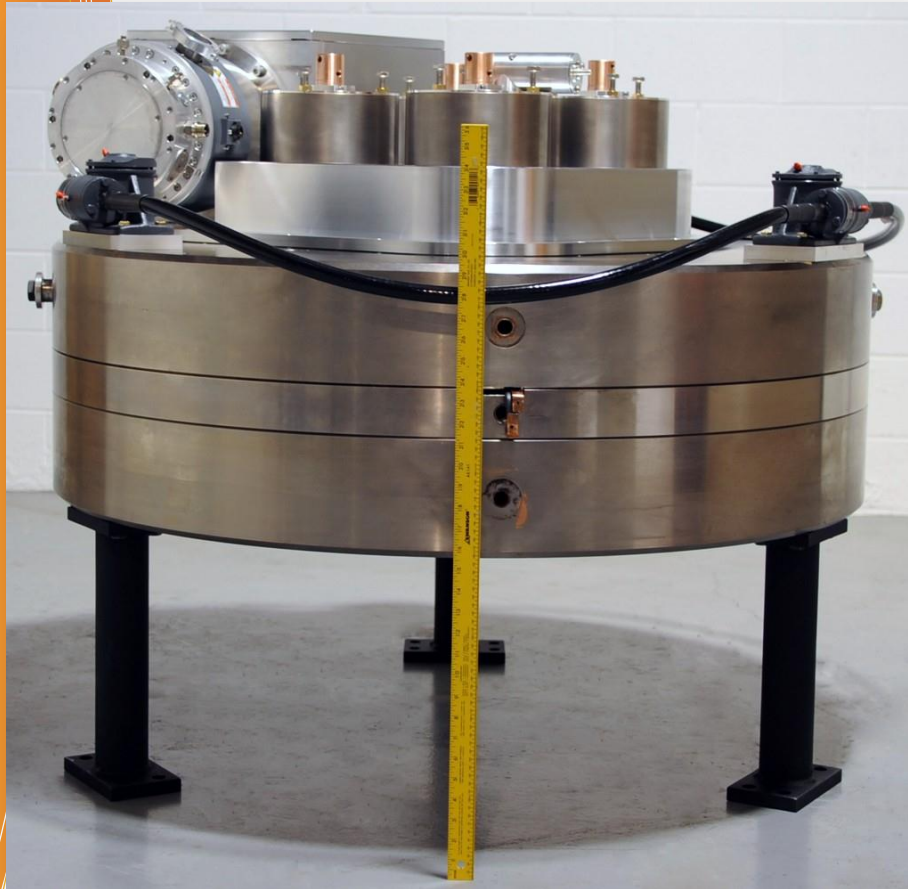


Important Characteristics

- Very low operating costs requirement.
- Fits into small room: 15' by 18' (4.5 m x 5.5 m).
- Requires minimal alterations of the facilities.
- Produces individual dose of FDG in 45 minutes with repetitive doses every 25 minutes.
- Produces all other important [^{18}F]fluoride-based research biomarkers (NaF, FLT, F-MISO) and C-11(future)
- Process is fully automated – one button operation.
- Meets Good Manufacturing Practice standards (CFR 21p11 compliant)



Accelerator Specifications



- 7.5 MeV Positive Ion Cyclotron
- 3 Internal targets
- Production Rate of 1.0 mCi/min [¹⁸F]fluoride
- 1.16 T Magnet
- 2-5 μ A Beam current
- 150 μ L Target Volume

Chemistry Production

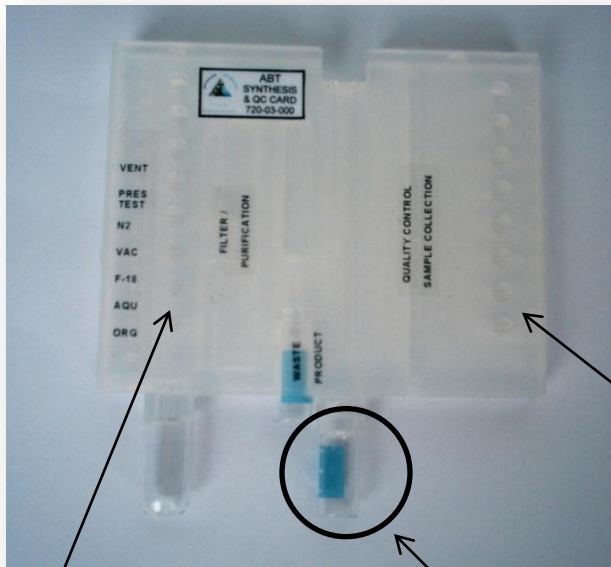


The Chemistry Production Module (CPM) controls the process for the conversion of one unit dose of biomarker.



The Dose Synthesis Card (DSC) manages Biomarker Synthesis of each patient dose, and the sampling for the Quality Control.

Dose Synthesis Card (DSC)



Single Use Disposable Card for Biomarker Synthesis

- Includes all wetted components and delivery lines
- Purification cartridge
- 0.22 μm sterile filter
- Internal waste containment

Biomarker Synthesis

Patient Dose

QC Sampling



FDG Synthesis Process

Step	Time (mm:ss)
Fluoride Activation	2:00
Fluorination	2:00
Solvent Removal	2:30
Hydrolysis	2:30
Purification	1:30
Dilution & Transfer	1:00
Total	11:30

Measure	Yield
n Runs	96
RCY (Labeling)	98 %
RCY (Hydrolysis)	95 %
Transfer Yield	85 %
Residual (Vessel - vial)	0.9 %
Residual (SPE / Filter)	3.0 %
Decay (Time)	8.0 %
Total Chemical Yield	79.9 ±5.0%



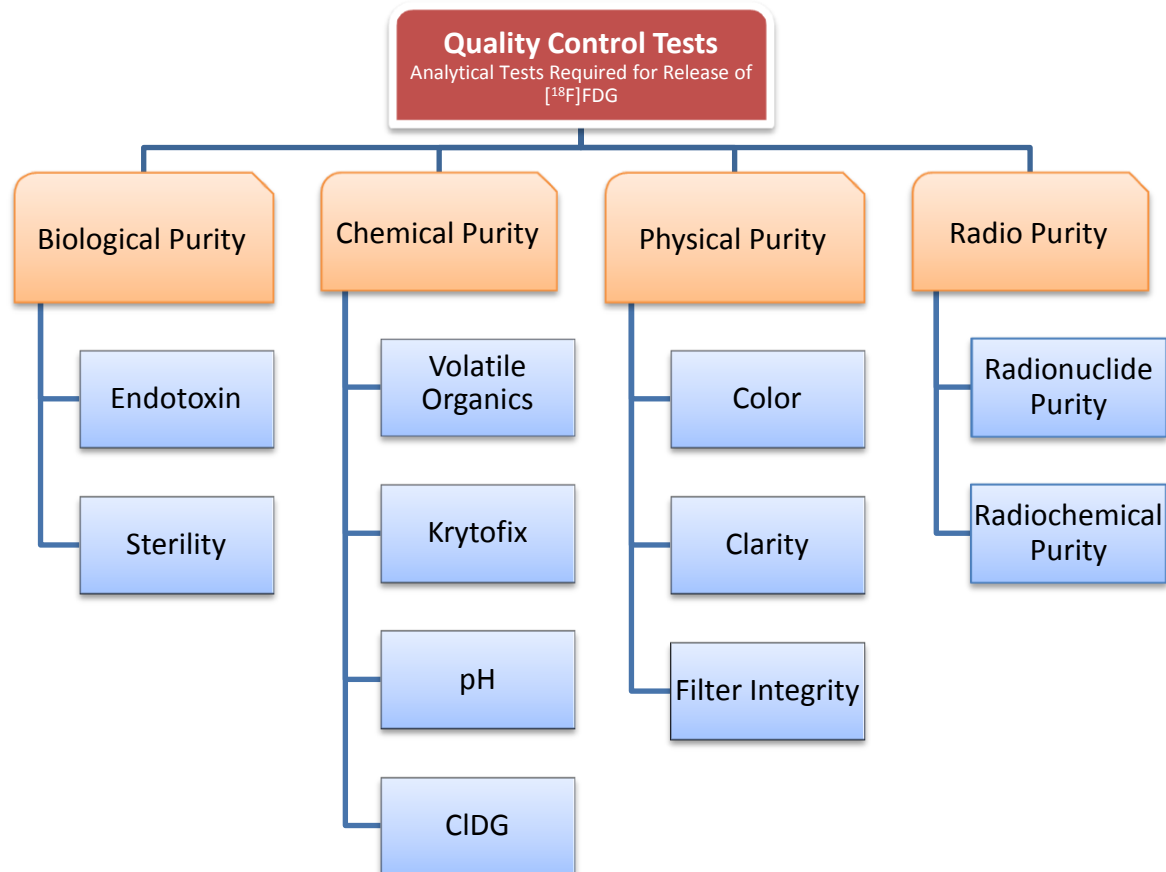
Integrated Quality Control



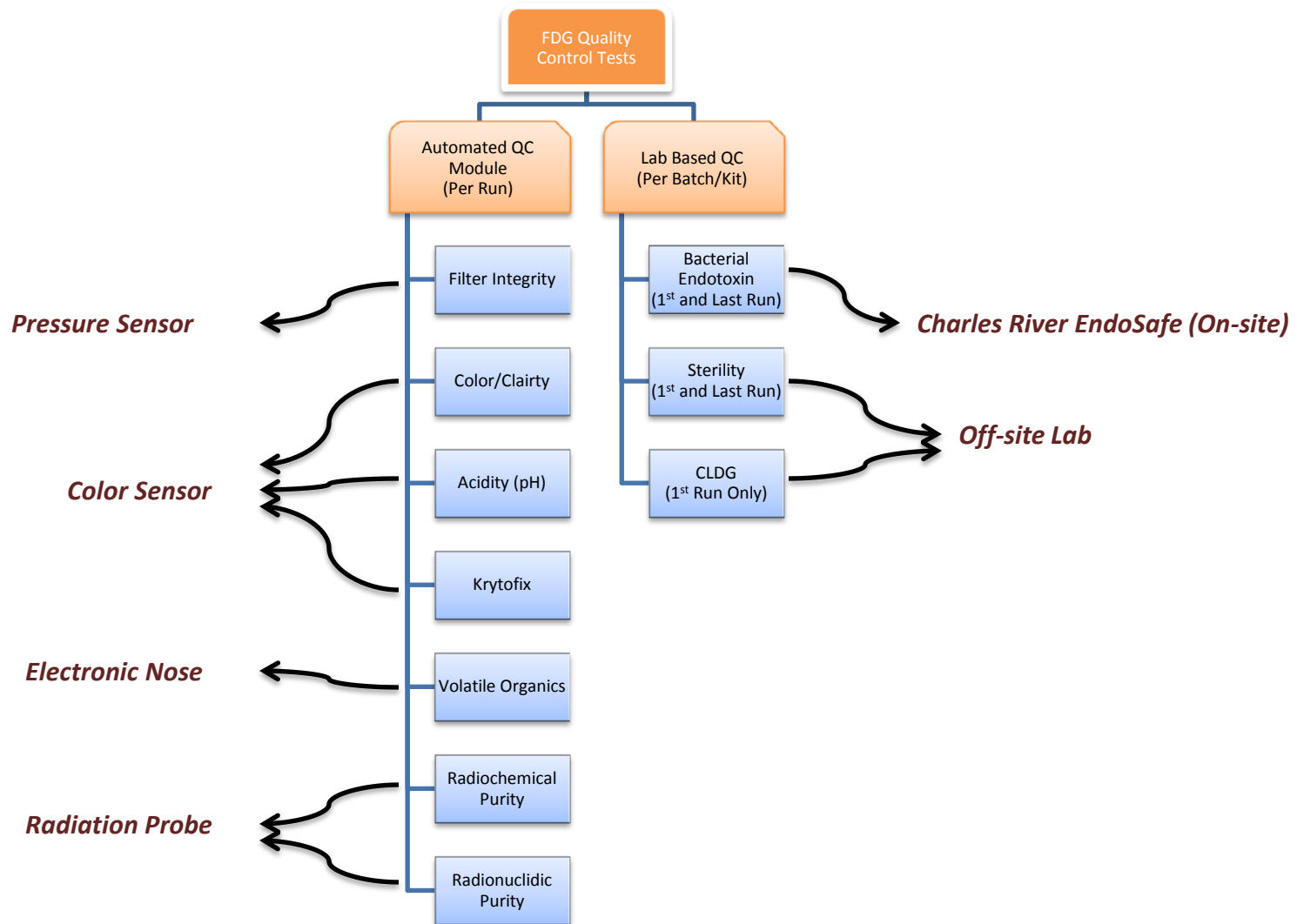
- Measures each dose to confirm that it meets Good Manufacturing Practice Standards
- Tests pH, kryptofix, organic solvents, purity, color, and clarity.
- Automated analysis using Optical, TLC, and Micromechanical Sensors
- A simple GO-NO-GO light indicates the results of the measurements for each dose.



FDG Quality Control Tests



Integrated Quality Control Tests



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Final Dose Record

ABT Biomarker Generator (BG)
[¹⁸F]FDG FINAL PRODUCT QC Test Results

Originator:	Anthony M. Giamis
Process Owner:	Anthony M. Giamis
Mgmt Approval:	
Q&R Approval:	

ABT# 615-99-1022 / Form M-001	
Revision:	A
Supersedes:	
Date Issued:	
Date Effective:	

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Dose Number: **MDR-¹⁸F**FDG-_____ Manufacturing Date: _____

Test Description	SOP Reference	Specification	Test Result(s)	Pass / Fail	Performed By/ Date	Supervisor Check By/ Date
Radiochemical ID & Purity (Radio-TLC)	QC-103	Rf > 0.5 Purity ≥ 95%	Rf = _____ Purity = _____%			
Residual Solvent (Gas Chromatography)	QC-104	Acetonitrile < 400 ppm	Acetonitrile = _____ ppm			
Radionuclidic ID (Half-Life Test)	QC-105	100-120 minutes	_____ min			
Bacterial Endotoxin (EndoSafe PTS)	QC-100	< 175 EU per dose	Pass Fail (Circle One)			
pH	QC-101	4.5 - 8	_____ pH			
Chemical Purity (K12.2.2) Color-spot Test)	QC-106	< 50 µg/mL Kryptofix	(> 50 µg/mL) (< 50 µg/mL) Positive Negative (Circle One)			
Chemical Purity (Particulates)	QC-102	Clear, Colorless, No particulates	Pass Fail (Circle One)			
Sterility*	QC-107	Negative/ No Growth	Pass Fail (Circle One)			

*Test Not Required for Preliminary Release

Attach all test results to this QC Form, corresponding to the testing performed for the batch referenced above.
Note any outstanding QC Investigations that are outstanding in the comment section below. For all doses, note the volume of each dose and ug in the dose in the comment section below.

Comments: _____

Preliminary Release By: _____ Date: _____
(Signature)

Dose Labels for Manufacturing Sites

Dose Record label:


Fludeoxyglucose [18F] Injection – [¹⁸F]FDG (Site name here)

Lot #: Dose Record # Date: Date Time: Time (EOS)

Activity: QC Measure mCi (QCM * 37) MBq in 2.0 mL @ EOS

Expiration Date: Date Time: EOS + 2 hrs Initials: _____

Diagnostic – For Intravenous Administration Only



Dose Product (Shield) label:

(Site name here) PET Radiopharmacy:

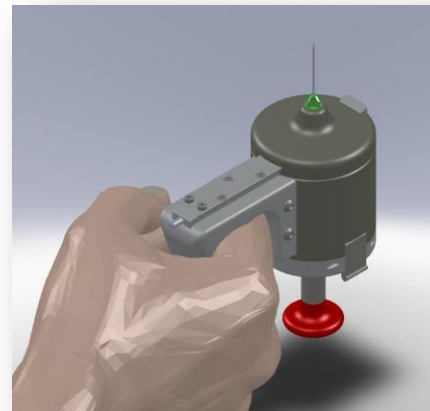
[¹⁸F]FDG, [¹⁸F]Fludeoxyglucose, 2-deoxy-2-[¹⁸F]fluoro-D-glucose in 0.9% saline.

MDR-¹⁸F)FDG Dose Record # _____ **Caution**

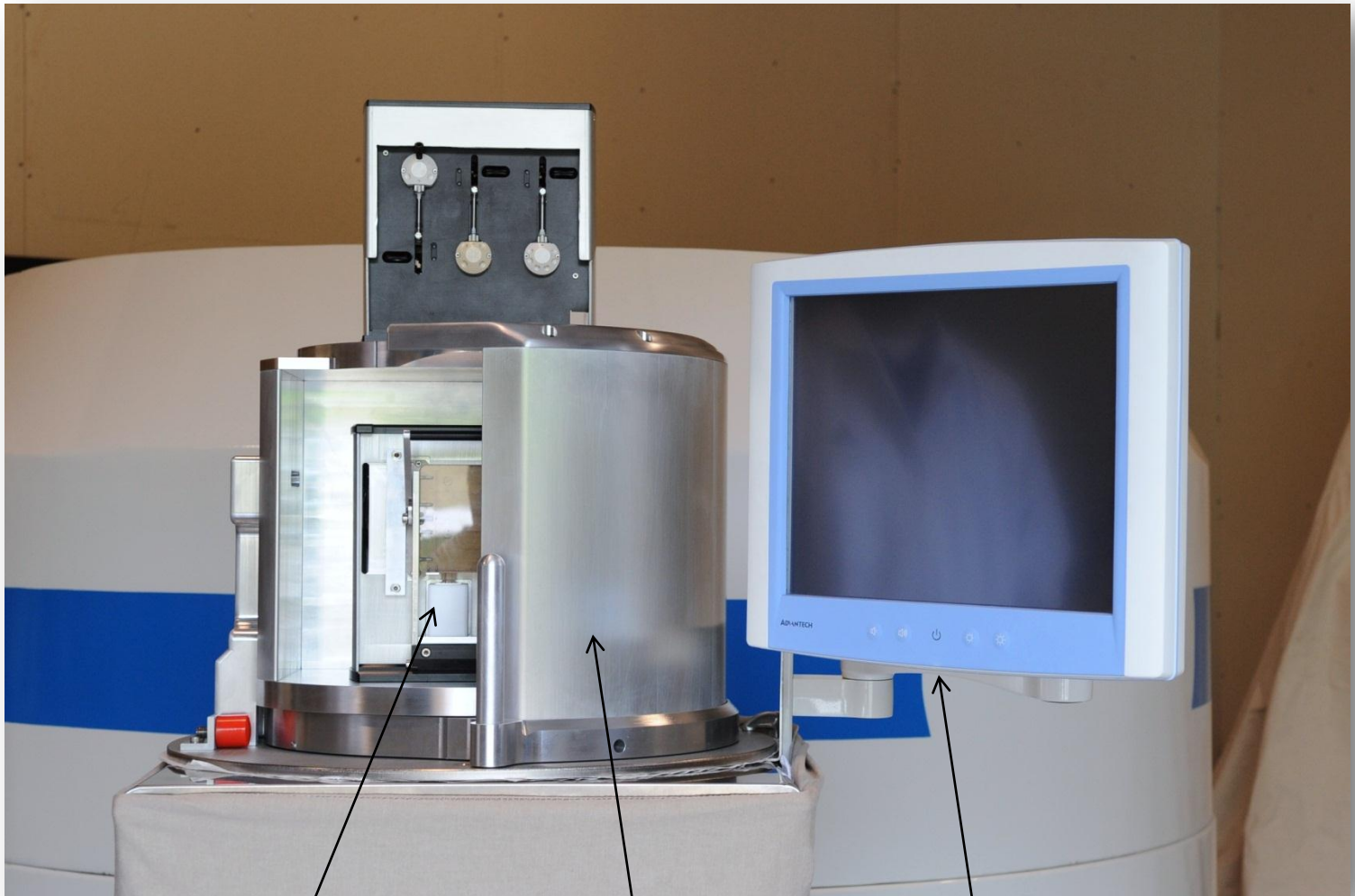
Activity: _____ mCi in _____ mL **Radioactive Material**

Calibration Date: _____ Time: _____

This radiopharmaceutical is for intravenous injection by prescription only. Do not use if cloudy or if it contains particulate matter. Expires 2 hours after calibration (EOS). Calculate injection dose from date & time of calibration. T_{1/2} is 109.8 minutes.



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Chemistry

Shield

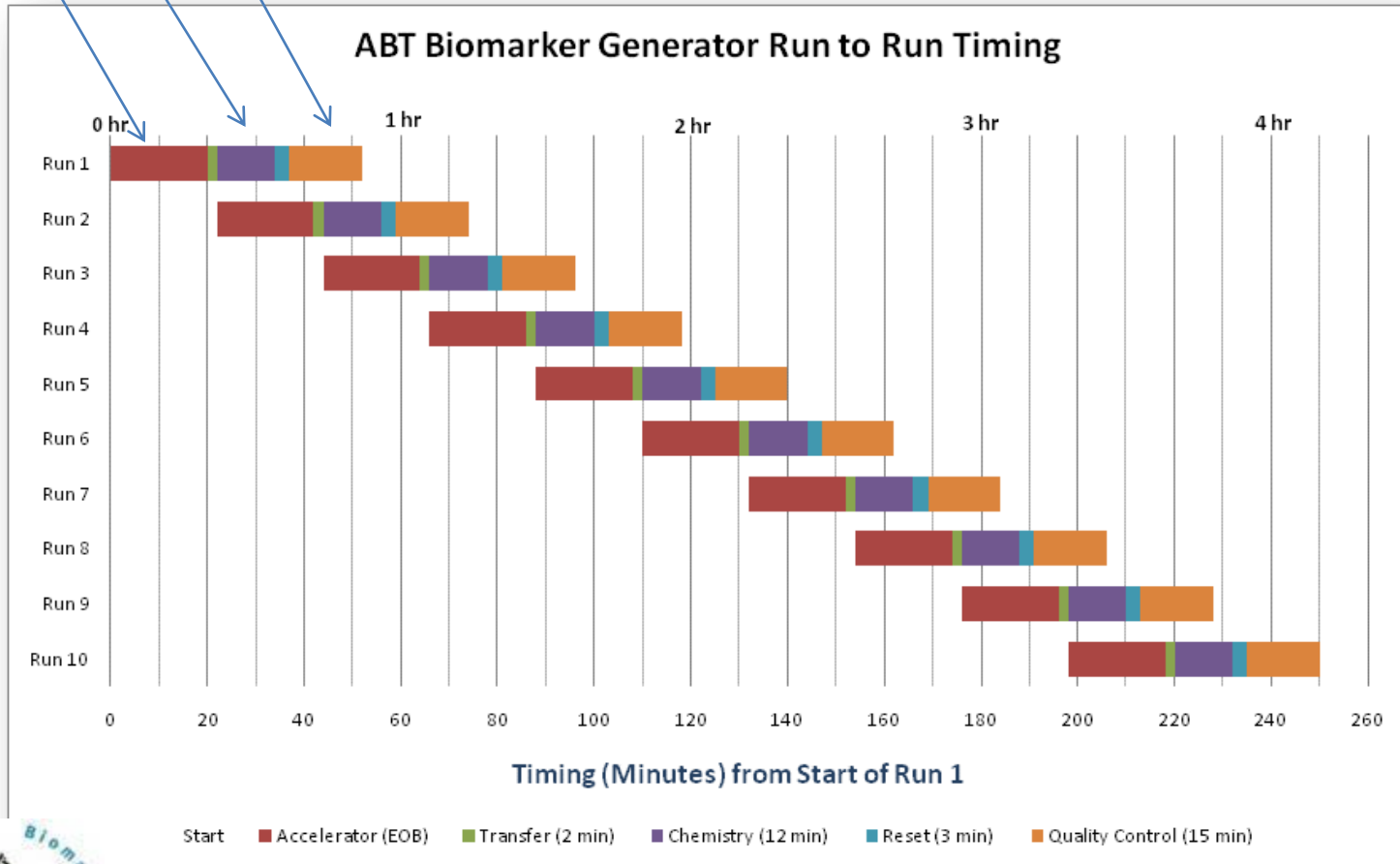
User Control



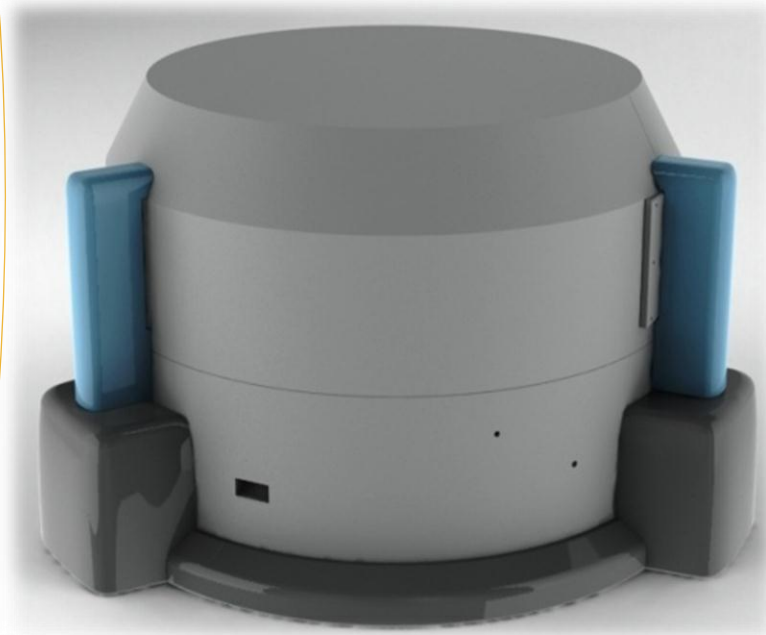
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"F-18 Production"
"FDG Chemistry"
"Quality Control"

FDG Dose produced every 25 minutes

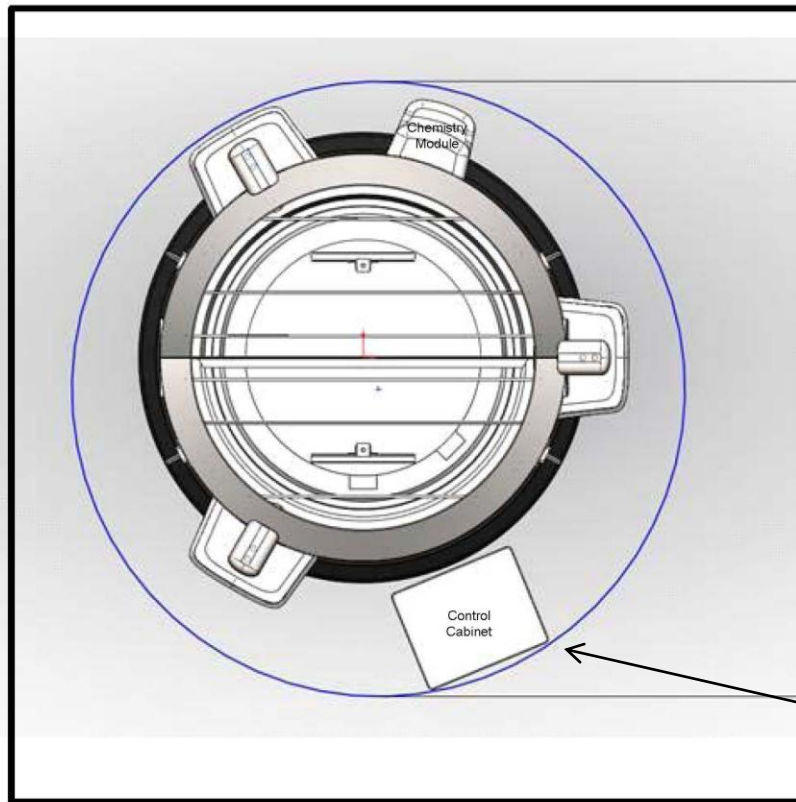


Shielding



- 8'3" diameter x 5'2" height
- Opens vertically for service access
- Bottom also shielded if needed
- Self Shielding requires no vault

Room Requirements



- 15' x 18' room
- 48" door entry for equipment entry
- 2.5 KW HVAC
- 208V, Single Phase
- 19T Total Weight
- <1 mR per hour at walls

Control Cabinet (Power supply)

"Dose-on-Demand"

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Features of the Biomarker Generator

Small Size:

- 18' X 15' (4.5m x 5.5m) room
- Minor facility modifications

Low Power:

- Low radiation burden
- Low operating costs
- Self shielded

Simple:

- Push button operation
- Embedded methods & processes
- Operated by existing staff

Cost effective:

- Access to advanced biomarkers for 20% of conventional cyclotron investment

