GMP Facilities at the NIH Clinical Center




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Clinical GMP Facilities

Pharmaceutical Development Service

Positron Emission Tomography

Cell Processing Service

Pharmaceutical Development Section

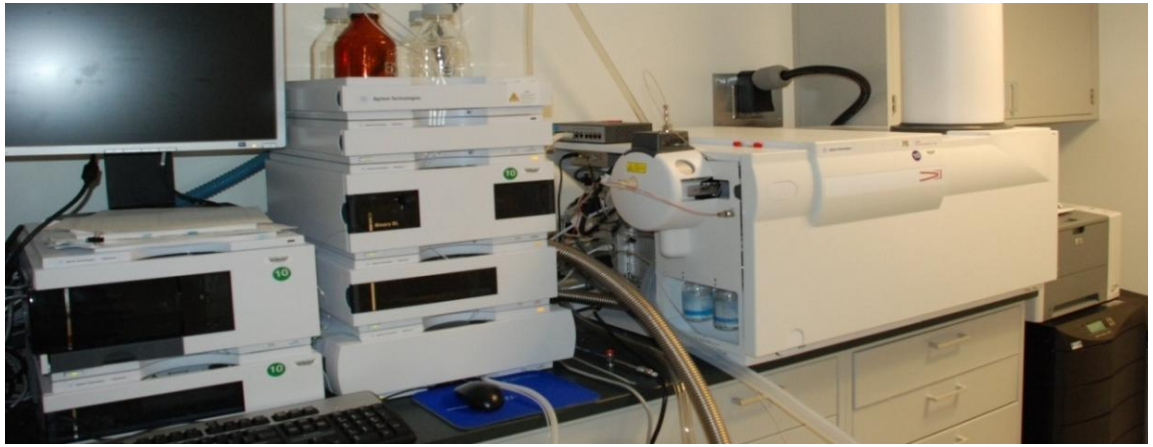
Pharmacy Department

George Grimes, RPh, BS Pharm, Chief

In existence sine 1956 - - - - New Facility 2010

Pharmaceutical Development Section

- Product Development
- Analytical and Quality Control
- Pharmacokinetics



Pharmaceutical Development Section Functions

- Responsible for ~1100 investigational drugs currently studied at the CC
- Formulates tablets, capsules, sterile parenterals, and topical products, including placebos
- Ensures that raw materials used and finished products are suitable for human use
- Maintains accountability records for sponsor and FDA review
- Assists in filing INDs

Manufacturing Capability
(8 hour day)

- 75,000 capsules
- 150,000 tablets
- 220 liters
- 5,000 syringes
- 8,000 vials (includes vaccines and biologics)

Capacity could be tripled by operating 3 shifts.

Department of Positron Emission Tomography

Peter Herschovitch, M.D., Chief

PET Resources

- **Three medical cyclotrons**
  - CS-30 (4-particle; 1985)
  - Two GE PETtrace cyclotrons

- **Radiochemistry**
  - 10 hot cells for synthesis of radiopharmaceuticals
  - Lab for radiopharmaceutical QC and dispensing

- **Scanners**
  - Three GE Advance whole body scanners (PET/CT scanner in procurement)
  - High Resolution Research Tomograph

Cyclotron Radionuclides

Standard PET nuclides

Radionuclide	Half-Life (min)
O-15	2
N-13	10
C-11	20.4
F-18	110

Other PET and non-PET nuclides (CS-30 cyclotron)

Radionuclide	Half-Life (hrs)
At-211	7.2
Br-76	16.2
Cu-60	0.40
Cu-64	12.7
Bi-205	367.4
I-124	100.2
Pb-203	51.9
Re-186	90.6
Sr-85	1556.1
Tc-94m	0.88
Y-86	14.7
Zr-89	78.4

PET Radiopharmaceuticals

[^{18}F]FDG	glucose metabolism (brain, body)
[^{15}O]water	blood flow (brain, body)
[^{18}F]FDOPA	presynaptic dopaminergic function (brain); NETs
[^{18}F]FDopamine	peripheral sympathetic function, NETs (body)
[^{13}N]ammonia	myocardial perfusion
[^{11}C]raclopride	dopamine D2 receptors (brain)
[^{11}C]palmitic acid	fatty acid metabolism
[^{11}C]arachidonic acid	second messenger via PI turnover (brain)
[^{18}F]FP-TZTP	muscarinic acetylcholine M2 receptors (brain)
[^{18}F]FCWAY	serotonin 5HT1A receptors (brain)
[^{11}C]carbon monoxide	blood volume (brain, body)
[^{11}C]flumazenil	benzodiazepine receptors (brain)
[^{11}C]docosahexaenoic acid	incorporation of DHA (brain)
[^{11}C]DASB	serotonin transporters (brain)
[^{11}C]DTBZ (2006)	VMAT2 (brain, body)
[^{11}C]leucine (2006)	protein synthesis rate (brain, body)
[^{94m}Tc]Sestamibi (2007)	MDR probe in cancer
[^{11}C]NNC (2007)	dopamine D1 receptors (brain)
[^{18}F]fallypride (2007)	dopamine D2 receptors (brain)
[^{11}C]acetate (2008)	prostate cancer (membrane lipid)
[^{11}C]carfentanil (2010)	opiate receptors (IND in preparation)

N = 21

PET GMP Facility

Purpose: Manufactures GMP radiopharmaceuticals

- **PET scans for patients under IRB-approved protocols**
- **21 PET radiopharmaceuticals currently available**
- **New GMP facility will replace 1985 facility**

New PET GMP Facility

- **Location:** 6,280 sq ft on the B3 level of CRC
- **Will include:**
  - Up to 19 hot cells to handle large (Ci) amounts of radioactivity
  - Clean room
  - Analytical laboratory for quality control
- **Capabilities:**
  - Meets FDA GMP regulations
  - Doubles current capacity
  - Extramural shipment of GMP F-18 radiopharmaceuticals (2-hour half-life)

Cell Processing Section
Department of Transfusion Medicine

David Stroncek, M.D., Chief

Mission:

Provides cellular and gene therapies

Cell Processing Section

Resources:

- Product Development Laboratory
- GMP Laboratory
- Regulatory affairs

Standard of Care Activities:

- Supports hematopoietic stem cell transplant programs

IND protocols for Phase I/II Clinical Trials Activities:

- Gene Therapy
- Dendritic Cells for Cancer Therapy
- Cytotoxic Cells for Cancer/Lymphoma Therapy
- Donor Leukocyte Infusions

NIH Bone Marrow Stromal Cell (BMSC) Transplant Center

Cell Processing Manufacturing Capability

- **12 hour days, 5 days a week**
  - **25 intense procedures could be performed each week; or**
  - **8 to 12 products could be produced per week**
- **24 hour days, 5 days a week**
  - **The capacity could be doubled to 16 to 24 products per week**
- **24 hour days, 7 days a week**
  - **The theoretical capacity is 23 to 35 products per week**

In Conclusion…

The Clinical Center's three GMP facilities support the NIH intramural programs but could be expanded to assist outside investigators.