# ORGANIZATIONAL/MANAGEMENT PLAN

* 1. Administration of the Instrument

The proposed instrument will be a central part of the biomedical research effort at the MGH. The proposed automated Ga-68 radiotracer production will be administered by the Institute for Innovation in Imaging, i3, within the MGH Department of Radiology. Dr. Peter Caravan and Dr. John Chen are Co-Directors of the i3. Dr. Peter Caravan will serve as Shared Instrument Director. Dr. Caravan will assume administrative and scientific oversight responsibility for this instrument and will be primarily responsible for ensuring that the facility is used in accordance with all i3, MGH and Federal guidelines, and that access to the instrument is provided to the MGH and regional research community. Dr. Philip Neilsen, a licensed radiopharmacist, will act as Technical Manager of the Shared Instrument. He will be responsible for the operation and administration of the instrument, system development and safety concerns. He will manage instrument operation, maintenance and upgrade, and safety, under the guidelines set forth by the Operations Committee.

# Scientific Advisory Committee

The role of the Scientific Advisory Committee for this shared instrument grant will be served by the senior core faculty and staff members within the Department of Radiology. This committee was established to advise the Institute for Innovation in Imaging during development and initial implementation. The committee meets monthly to discuss a wide range of topics focused on activity at the Insitute for Innovation in Imaging, including management, maintainence and access to shared resources such as the proposed instrument. The Scientific Advisory Committee will be responsible for the annual report to NIH that will detail usage of the instruments. During the compilation of the annual report, the Technical Director will contact the Prinicipal Investigators who have used the instrument in the last year and remind them to associate the grant for this instrument with their publications as appropriate.

# Table 4. Scientific Advisory Committee

|  |  |
| --- | --- |
| Peter Caravan, PhD (non-voting) | Director, Institute for Innovation in Imaging |
| Ciprian Catana, PhD | Director, PET Core, Martinos Center |
| Bruce Fischl, PhD | Director, Computational Core, Martinos Center |
| Jacob Hooker, PhD | Director of Radiochemistry, Martinos Center |
| John Chen, MD, PhD | Director, Institutue for Innovation in Imaging |
| Monica Langone | Senior Administrative Manager, Martinos Center |
| Umar Mahmood, MD | Director of the Division of Precision Medicine, Martinos Center |
| J. Matthew Dubach, PhD | Associate Director, Institute for Innovation in Imaging |
| Ralph Weissleder, MD, PhD | Director, Center for Systems Biology |
| Bruce R. Rosen, MD, PhD | Director, Athinoula A. Martinos Center for Biomedical Imaging |
| William H. Shaw, JD | Executive Director, Athinoula A. Martinos Center for Biomedical  Imaging |
| David Sosnovik, MD, FACC | Medical Director, Institute for Innovation in Imaging |
| Steven Stufflebeam, MD | Medical Director, Martinos Center |
| Lawrence L. Wald, PhD | Director, Martinos NMR Core, Martinos Center |

Users of the instrument are in red font.

The committee will provide direct oversight for Ga-68 radiotracer production, leveraging their deep experience in PET imaging, radiochemistry and shared instrument management. Peter Caravan, Ph.D., Director of the Instititute for Innovation in Imaging is ultimately responsible for all cGMP operations including resource scheduling, staffing, vendor interactions, maintenance, etc., in accordance with the policies and decisions of the Scientific Advisory Committee and the Department of Radiology administration. In addition, the Institute for Innovation in Imaging works closely wth the MGH Radiation Safety Office, Tara Medich Director, to ensure a safety and operations training program is properly developed and disseminated for the Ga-68 radiosynthesis facility.

Requests for production runs on Ga-68 automated radiotracer production system will be administered via the Martinos Center website and in accordance with established policies for time allocation. The system electronically records the run and usage time required for each production run and automatically charges the appropriate account, project, and grant. The Technology Core Administrator, Karen Dervin, oversees all

aspects of instrument scheduling, and billing. See letter of support from Dr. Rosen, Director of the Martinos Center, attesting that scheduling for the Ga-68 automated radiotracer production system will be administered by Ms. Dervin and the automated Martinos scheduler.

The investigator can reserve a run slot for a single use or a fixed time for up to 3 months after all necessary documentation and experimental design has been performed. If the radioligand will be used for imaging studies, the reserved times at the Institute for Innovation in Imaging facility and the PET imaging device must be synchronized, so that the PET imaging facility is available immediately after the radioligand is cleared following pharmacological testing for use. The Institute for Innovation in Imaging will be connected to the Martinos reservation system for PET imaging instruments to avoid confusion or delays. Ms. Dervin, the administrator, oversees both systems to insure that imaging and radiochemistry are scheduled together.

All users of the Institute for Innovation in Imaging facilities are required to complete the System Operation and Safety Training course and provide documentation certifying completion of institutional training on human subject research (e.g., CITI, HIPAA) prior to receiving a login account for a project. Prior to gaining access to the instrument, all human and animal studies must be approved by the Partners Human Research Committee and/or the Subcommittee on Research Animal Care, respectively, which evaluate the proposals for scientific, experimental, and ethical considerations. Projects are also screened by the SAC for scientific content, appropriateness of instrument use, and adequacy of user training and animal studies institutional approval.

# Policy for Allocation of Instrument Resources

The PHS-funded projects described in this application will constitute at least 80% of radiolabeling performed in the proposed instrument. Of the remaining 20% of the instrument, eight percent will be reserved for educational and training purposes and seven percent for preliminary or developmental (pilot) work showing strong potential for future PHS funding. Applications for the pilot/development work will be reviewed by the Scientifc Advisory Committee on a bi-monthly basis. Five percent of the instrument time will be reserved for routine instrument quality assurance, maintenance and repair procedures.

Under the standard scheduling scheme, users may request of up to six scheduled production runs in a one- month period, and slots cannot be requested more than 3 months in advance. New requests for production runs are solicited and new schedules are posted every 3 to 4 months. These activities are carried out through the Institute for Innovation in Imaging web-based scheduling system, in synchrony with the Martinos PET imaging reservation system. The Technology Core Administrator, Karen Dervin, oversees all aspects of instrument scheduling, and billing. These policies allocate the majority of imaging time to the direct support of PHS and NSF funded users and for projects funded by other funding agencies, including pilot work supported by the Institute for Innovation in Imaging and other institutional funds. The remaining time is reserved for routine instrument quality assurance and maintenance and repair procedures.

Identification of new projects. We will advertise the availability of the Ga-68 automated radiotracer production system to potential new users in three ways. First, this will be publicized on the i3 website, the i3 Core Services website, and links to the i3 Core will be made from the website that lists all core services at HMS, MGH, and Brigham and Women’s Hospital. Second, each year there is a Mass General Brigham system wide Core day where Research Cores present the services and facilities that they offer and this is an effective way to reach new researchers. Finally, the i3 routinely performs outreach within MGH Radiology to make researchers aware of the services that are offered and we will include the Ga-68 automated radiotracer production system.

# Financial Administration

**Long-term costs of the automated Ga-68 radiolabeling system**

The proposed instrument will be administered on a fee-for-service basis, as are other existing imaging and radiochemistry production resources at the Institute for Innovation in Imaging. Investigators will pay a "per use" rate calculated to cover the operating, consumable and maintenance costs of the proposed instrument and related expenses. The rate is calculated on a per-run basis, based on the total costs of operation (including the salaries of relevant technical support staff, equipment service, and supplies) divided by the total estimated production runs. Costs will be supported on an ongoing basis by the broad portfolio of PHS funded and other funded research programs. In addition, the Institution through the MGH Executive Committee on Research (ECOR) has committed to contributing institutional funds in the amount of $100,000, as attested to in the letter supplied by the Hospital’s Senior Vice President for Research, Dr. Harry Orf. This additional $100,000 is

earmarked to support operational costs (e.g. consumable supplies), maintenance (e.g offset service contract), and provides a buffer to support the technical staff should our billable batch production estimate prove too high especially in the first year of operation when projects are onboarding. Though not anticipated, the Institute for Innovation in Imaging and Radiology Department have committed the necessary financial support to cover unexpected budget shortfalls during any period (see Section F. Institutional Commitment and letter from Dr. Brink, Chair of Radiology). Note that Table 5 is conservatively budgeted to run at a small surplus. These projections will be revisited each year such that if there is a surplus, fees will be reduced and if there is a deficit the core may increase fees to make the operation cost neutral. The current cost for a non-FDG human use tracer is $2310 per dose (see https://[www.nmr.mgh.harvard.edu/core).](http://www.nmr.mgh.harvard.edu/core)) For preclinical and development use we have set a fee of $400 per production and to obtain Ga-68 for other research a fee of $100. We anticipate 3 human studies involving a Ga-68 tracer, approximately 4 preclinical and development productions and 1 other research need per week with this system. This mix of clinical and development/preclinical is likely to shift to more clinical studies as the new probes come on-line.

We anticipate that the addition of this instrument will not only allow existing studies to meet their research goals, but also foster the development and ultimate funding of new projects, and as such will serve as an important mechanism for growing and evolving translational imaging research at the Institute for Innovation in Imaging on a broad scale.

# E 3.1. User Fee Calculation

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Table 5: Estimated Annual Instrument Revenue and Operating Costs, Years 1 - 5** | | | | | |
| **% effort IBS salary Salary** | | | | **Benefits** | **Annual Cost** |
| **PERSONNEL** |  |  |  |  |  |
| Technical Director | 40 | 150,000 | 60,000 | 21,000 | $81,000 |
| Radiochemist | 50 | 60,000 | 30,000 | 10,500 | $40,500 |
| Research Technician | 100 | 48,000 | 48,000 | 16,800 | $64,800 |
|  |  |  |  |  | **-$186,300** |
| **OPERATING COSTS** |  |  |  |  |  |
| Consumables ($1,000/GMP & $200/dev, pre) |  |  |  |  | $186,000 |
| cGMP compliance maintainence ($10,000 |  |  |  |  | $35,000 |
| plus $500/week of operation). |  |  | |  | |
| Software upgrades, maintenance contract |  |  | | $30,000 | |
|  |  |  | | **-$251,000** | |
| **Anticipated Income** | runs | Fee, /run | |  | |
| Human production (GMP) | 140 | $2310 | | **$323,400** | |
| Development and preclinical research | 230 | $400 | | **$92,000** | |
| Other research | 30 | $100 | | **$3,000** | |
| Institutional support\* |  |  | | **$20,000** | |
|  |  |  | | **$438,400** | |
| **NET TOTAL** |  |  | | **$1,100** | |

\* MGH ECOR (see letter of support from Dr. Orf, SVP of Research) has committed $100,000 to this project to cover maintenance and operating costs. We apply this as $20,000 per year over the 5 year period.

Our total capacity at 2 productions/day for 5 days a week (weekend access is restricted because GMP production will be in a controlled facility) or approxiametly 500 total productions per year when considering maintenance time. Based on previous productions we also expect consumables to cost $1,000 per GMP production and $200 per development and preclinical production. GMP production is only capable through leveraging the significant resources provided by MGH and the Department of Radiology. The total anticipated

productions is derived from expected need of each project. The conservative estimate results in 400 total productions/year corresponding to a 80% usage level. This is similar to other radiochemistry facilities and provides flexibility for unexpected maintenance or other issues.

We have modeled this on a 5 day a week, 2 productions per day model. Should demand grow, we will be able begin the workday earlier and add a 3rd production per day. In addition, if the need arises we can provide additional training to make the facility available to researchers for non GMP use on weekends. The low cost of development access to the insrument ($400/production), which provides for a half day of access, enables new research and projects to be performed with little financial burden.

We estimate 400 billable productions per year for this new system, given time for system development, pilot studies for this new system, and routine maintenance and repairs. We estimate initially about 140 (~3 per week) GMP productions to support clinical studies and these are billed at $2310 in line with existing pricing at MGH for non-standard PET tracers. We anticipate another 230 non-GMP productions performed for development purposes or to support preclinical studies. Rates are calculated on a per-production basis, based on the total costs of operation (including the salaries of relevant technical support staff, equipment service, and supplies) divided by the total estimated billable runs. Therefore, non-GMP develop and preclinical use will have access to the instrument and Ga-68 source for half a day for each production. Based on our annualized cost estimates for operating the device (Table 5), and an annualized paid usage of the machine at 140 GMP productions, 230 non-GMP productions and 30 Ga-68 source productions every year fees are estimated to be

$400/production for the non-GMP productions and $100/production as a Ga-68 sourse. This billing structure will provide $418,400 per year and, combined with institutional support, will cover the operating costs associated with this instrument. This rate is periodically reviewed by both the Insititute for Innovation in Imaging Scientific Advisory Committee and MGH Research Administration, and adjusted to reflect the actual costs and usage. In addition, the Institution through the MGH Executive Committee on Research (ECOR) has committed to contributing institutional funds in the amount of $100,000, as attested to in the letter supplied by the Hospital’s Senior Vice President for Research, Dr. Harry Orf. This additional $100,000 is earmarked to support operational costs and maintenance. Note that Table 5 is conservatively budgeted to run at a small surplus. This will be revisited each year such that if there is a surplus, fees will be reduced and if there is a deficit the core may increase fees to make the operation cost neutral.

# Time Frame for Delivery

The time frame for delivery of the hot cells is 6 months after receiving the order. The time frame for delivery of the PharmTracer/GalliaPharm is 3 months. We anticipate a period of two months to acceptance of the system from its shipment. Therefore, given receipt of notice of award in February of 2021, we anticipate delivery and installation of the entire system around October of 2021. While we based our application on the system from Eckard-Ziegler, if we are funded we will conduct a thorough evaluation of alternative vendors such as Capintec or IRE and potentially other new vendors in the future as technology, performance and cost evolve with time.

# Table 6: Timeline for System Installation Month Installation Progress

0 Place order for hot cells

3 Place order for PharmTracer/GalliaPharm

6 Hot cells/PharmTracer/GalliaPharm delivered

8 Installation and testing of the instrument and combined functionality complete