



March 25, 2021

U.S. Nuclear Regulatory Commission, Region III
Materials Licensing Branch
2443 Warrenville Road, Suite 210
Lisle, IL 60532-4352

Attn: Bryan Parker
Re: Change in RSO and Authorized User for License #21-03298-06

This is a follow-up to our earlier letter dated 12/16/2020 regarding the RSO change for license number 21-03298-06. Please find attached the RSO appointment letter.

We also request a change in Authorized User from Thomas Mangner to Huailei Jiang, Ph.D. Supporting documentation of training and experience is attached.

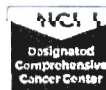
Sincerely,

A handwritten signature in black ink, appearing to read "Mara Jelich".

Mara Jelich
Executive Director, Radiation Oncology and Imaging
Karmanos Cancer Center
4100 John R St., Mail Code GE00RO
Detroit, MI 48201
(313) 576-9555

2 Attachments
1) RSO Appointment Letter
2) AU Training and
Experience

4100 John R
Detroit, Michigan 48201
(800) KARMANOS (1-800-527-6266)
info@karmanos.org | www.karmanos.org





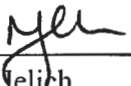
Memo To: Radiation Safety Officer

March 25, 2021

From: Executive Director, Radiation Oncology and Imaging

Subject: Delegation of Authority

You, Joseph T. Rakowski, have been appointed Radiation Safety Officer for NRC license number 21-0.298-06 and are responsible for ensuring the safe use of radiation. You are responsible for managing the Radiation Protection Program; identifying radiation protection problems; initiating, recommending, or providing corrective actions; verifying implementation of corrective actions; stopping unsafe activities; and ensuring compliance with regulations. You are hereby delegated the authority necessary to meet those responsibilities, including prohibiting the use of byproduct material by employees who do not meet the necessary requirements and shutting down operations where justified to maintain radiation safety. You are required to notify management if staff does not cooperate and does not address radiation safety issues. In addition, you are free to raise issues with the Nuclear Regulatory Commission at any time. It is estimated that you will spend 4 hours per week conducting radiation protection activities.

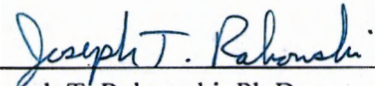


Mara Felich
Executive Director, Radiation Oncology and Imaging
Karmanos Cancer Center

3/25/21

Date

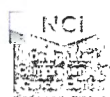
I accept the above responsibilities.



Joseph T. Rakowski, Ph.D.

3/25/2021

Date



Training and Experience of Huailei Jiang, Ph.D.

During the period February 22 through March 19, 2021, I supervised 40 hours of training to Dr. Jiang in the following topics:

- Radiation protection principles
- Characteristics of ionizing radiation
- Units of radiation dose and quantities
- Radiation detection instrumentation
- Biological hazard of exposure to radiation appropriate to types and forms of material used in positron emission tomographic imaging
- Handling of radioactive materials relevant to accelerator activities.

Dr. Jiang's experience includes the following:

Isotope hands-on experience and typical amounts:

- Fluorine-18: 10 Ci at end of beam and 6 Ci FDG in the final product at end of synthesis
- Carbon-11: 3 Ci at end of beam and 1 Ci in the final product at end of synthesis
- Gadolinium-68: 100 mCi at end of synthesis
- Zirconium-89: 20 mCi at end of synthesis
- Zinc-63: 50 mCi at end of synthesis

Mayo Clinic, FL

2018 to 2020

Senior PET Radiochemist/ Assistant Professor of Radiology

- Validation of PET drug production for ANDA application; prepared for FDA's Pre-Approval Inspection (PAI) and received FDA approvals (F-18 FOG, C-11 Choline, N-13 Ammonia and F-18 Sodium Fluoride).
- Validation for IND PET drug: C-11 PIB/C-11 PK11195 and F-18 FDOPA/F-18 AV 1451.
- Quality assurance activities, including continuous improvement on PET drug production process and quality control method; responsible for approval/release PET drug for clinical use.

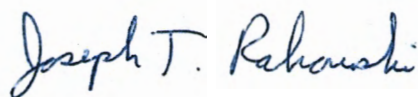
Mayo Clinic, MN

2013 - 2018

Research Associate/Senior Research Fellow/Research Fellow

- Successful translation of novel radiotracers for IND studies, such as F-18 TFB for thyroid cancer and oncolytic virus reporter gene imaging.
- Development of F-18 FMISO analogs for hypoxia imaging.
- Novel F-18 radiochemistry development including production and transport of gaseous F-18-synthons.
- Involve solution target production of radiometals (Ga-68, Zr-89, Zn-63) and chelation development.

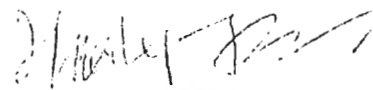
Dr. Jiang's signed CV is attached.



Joseph T. Rakowski

Karmanos Cancer Center RSO, License # 21-04127-06

Date of Preparation: 03/24/2021



Signature

Huailei (Ray) Jiang, Ph.D

Office Address: Karmanos Cancer Institute
4100 John R St.
Mail Code CH00PT
Detroit, MI 48201

Office Telephone: 313-576-9918

E-mail Address: jiangh@karmanos.org

Educations

Mayo Clinic, MN	Research Fellow, PET Radiochemistry	2013 - 2016
University of Chinese Academy of Sciences	Ph. D, Medicinal Chemistry	2006 - 2012
Anhui Normal University	B.S, Applied Chemistry	2002 - 2006

Professional Experiences

Karmanos Cancer Institute/Wayne State University, MI 2020 to present
**Scientific Director and Senior PET Radiochemist of Cyclotron and
Radiochemistry Core/Associate Professor of Oncology/Chair of RDRC**

- Development of C-11 and F-18 labeled PET drugs for the precise diagnosis of cancer, heart and brain related diseases within theranostic concept.
- Supervision of cGMP manufacturing of PET drugs, including various (A)NDA, IND and RDRC PET drugs.

Mayo Clinic, FL 2018 to 2020
Senior PET Radiochemist/Assistant Professor of Radiology

- Validation of PET drug production for ANDA application; prepared for FDA's Pre-Approval Inspection (PAI) and received FDA approvals (F-18 FDG, C-11 Choline, N-13 Ammonia and F-18 Sodium Fluoride).
- Validation for IND PET drug: C-11 PIB/C-11 PK11195 and F-18 FDOPA/F-18 AV1451.
- Quality assurance activities, including continuous improvement on PET drug production process and quality control method; responsible for approval/release PET drug for clinical use.

Mayo Clinic, MN 2013 - 2018
Research Associate/Senior Research Fellow/Research Fellow

- Successful translation of novel radiotracers for IND studies, such as F-18 TFB for thyroid cancer and oncolytic virus reporter gene imaging.
- Development of F-18 FMISO analogs for hypoxia imaging.
- Novel F-18 radiochemistry development including production and transport of gaseous F-18-synthons.
- Involve solution target production of radiometals (Ga-68, Zr-89, Zn-63) and chelation development.

- 1) Jiang H, Fang P, et.al. Analysis of [^{11}C]Choline and [^{13}N]Ammonia using a single HPLC method. *Applied Radiation and Isotopes*, 2021, 168, 109560.
- 2) Vandergaast R, Khongwichit S, Jiang H, et. al. Enhanced noninvasive imaging of oncology models using the NIS reporter gene and bioluminescence imaging. *Cancer Gene Therapy*, 2020, 27 (3), 179-188
- 3) Jiang H and DeGrado T. ^{18}F -Tetrafluoroborate (^{18}F -TFB) and Its Analogs for PET Imaging of the Sodium/Iodide Symporter. *Theranostics*, 2018, 8 (14), 3918.
- 4) Jiang H, Bansal A, et.al. Synthesis and evaluation of ^{18}F -Hexafluorophosphate as a novel PET tracer for imaging of Sodium/Iodide Symporter in a Murine C6-Glioma Tumor Model. *Bioorganic & Medicinal Chemistry*, 2018, 26, 225-231.
- 5) Brunton B, Suksanpaisan L, Li H, Liu Q, Yu Y, Vrieze A, Zhang L, Jenks N, Jiang H. et al. New transgenic NIS reporter rats for longitudinal tracking of fibrogenesis by high-resolution imaging. *Scientific reports*, 2018, 8, 1-9.
- 6) Jiang H, Schmit RN, et.al. Safety, Pharmacokinetics, Metabolism and Radiation Dosimetry of ^{18}F -Tetrafluoroborate (^{18}F -TFB) in Healthy Human Subjects. *European Journal of Nuclear Medicine and Molecular Imaging Research*, 2017, 7, 90.
- 7) Jiang H, Bansal A, et.al. Synthesis of ^{18}F -Tetrafluoroborate (^{18}F -TFB) via Radiofluorination of Boron Trifluoride and Evaluation in a Murine C6-Glioma Tumor Model. *Journal of Nuclear Medicine*, 2016, 57, 1454-1459.
- 8) Hickey R, Mao S, Glorioso J, Elgilani F, Amiot B, Chen H, Rinaldo P, Marler R, Jiang H, et.al. Curative ex vivo Liver-directed Gene Therapy in a Pig Model of Hereditary Tyrosinemia Type 1. *Science Translational Medicine*, 2016, 8, 349ra99
- 9) DeGrado T, Kemp B, Pandey M, Jiang H, et.al. First-in-human PET Imaging of ^{63}Zn -zinc Citrate in Healthy Elderly Subjects and Patients with Alzheimer's Disease. *Molecular imaging*, 2016, 15, 1-10.
- 10) Jiang H, DiMaggio S, DeGrado T. Production and Transport of Gaseous ^{18}F -Synthons: ^{18}F -Acyl Fluorides. *Journal of Fluorine Chemistry*, 2015, 180, 181-185.
- 11) Ou-Yang J, Zhao Y, Jiang H, et.al. A Simple, One-Pot Synthesis of Trans-Substituted Spiro [5, 5] undecane-1, 5, 9-triones with Aromatic Aldehydes and Meldrum's Acid as the Starting Materials. *Australian Journal of Chemistry*, 2015, 68, 1599-1602.
- 12) DeGrado T, Pandey M, Byrne J, Engelbrecht, H, Jiang H, et.al. Preparation and Preliminary Evaluation of ^{63}Zn Citrate as a Novel PET Imaging Biomarker for Zinc. *Journal of Nuclear Medicine*, 2014, 55, 1348-1354.
- 13) Pandey M, Byrne JF, Jiang H, et.al. Cyclotron Production of $(68)\text{Ga}$ via the $(68)\text{Zn}(p,n)(68)\text{Ga}$ Reaction in Aqueous Solution. *American Journal of Nuclear Medicine and Molecular Imaging*, 2014, 4, 303-310.
- 14) Domingo-Musibay E, Allen C, Kurokawa C, Hardcastle J, Aderca I, Msaouel P, Bansal A, Jiang H, et.al. Measles Edmonston Vaccine Strain Derivatives Have Potent Oncolytic Activity against Osteosarcoma. *Cancer Gene Therapy*, 2014, 21, 483-490.

- 15) Huang L, Lu C, Sun Y, Mao F, Luo Z, Su T, Jiang H, et.al. Multitarget-Directed Benzylideneindanone Derivatives: Anti- β -Amyloid ($A\beta$) Aggregation, Antioxidant, Metal Chelation, and Monoamine Oxidase B (MAO-B) Inhibition Properties against Alzheimer's Disease. *Journal of Medicinal Chemistry*, 2012, 55, 8483-8492.
- 16) Shan W J, Huang L, Zhou Q, Jiang H, et. al. Dual β_2 -Adrenoceptor Agonists-PDE4 Inhibitors for the Treatment of Asthma and COPD. *Bioorganic Medicinal & Chemistry Letters*, 2012, 22, 1523-1526.
- 17) Jiang H, Wang X, et. al. Benzenediol-berberine Hybrids: Multifunctional Agents for Alzheimer's Disease. *Bioorganic & Medicinal Chemistry*, 2011, 19, 7228-7235.

Abstracts

Oral presentations

- 1) Jiang H, Jain M and Cai. H. Analysis of [^{11}C]Choline Using High Pressure Ion Chromatography System (HPIC) with Autosampler. *Journal of Nuclear Medicine*, 2019, (supp) S639.
- 2) Jiang H, Schmit N, et.al. cGMP Synthesis of Sodium-Iodide Symporter (NIS) Probe ^{18}F -Tetrafluoroborate (^{18}F -TFB) and Biodistribution in Healthy Male and Female Human Subjects. *Journal of Nuclear Medicine*, 2017 (supp) S682.
- 3) Jiang H, Bansal A, et.al. First Synthesis of [^{18}F]Hexafluorophosphate and In Vivo Evaluation as PET Reporter Probe for Sodium/Iodide Symporter Imaging. *Journal of Labelled Compound and Radiopharmaceuticals*, 2017 (suppl) S60.
- 4) Jiang H, DeGrado T. Acyl [^{18}F] Fluorides as Novel Synthons for Radiofluorination *Journal of Nuclear Medicine*, 2014 (suppl) S161.

Posters

- 1) Jiang H, Fang P, et.al. Kill two birds with one stone: Analysis of [^{11}C]choline and [^{13}N]ammonia with a single HPIC method. *Journal of Nuclear Medicine*, 2020, (supp) S1001.
- 2) Jiang H, Fairweather D, et.al. Improved Production of (R)-[^{11}C]PK11195 for PET Imaging of Inflammation. *Journal of Nuclear Medicine*, 2020, (supp) S1004.
- 3) Zhong J, Zhang L, Jiang H, et.al. High Resolution Longitudinal Monitoring of HSC Transplantation Using the NIS Reporter Gene and PET/CT Imaging. *Molecular Therapy*, 2017, (suppl) S308.
- 4) Jiang H, Bansal A, et.al. Synthesis of ^{18}F -Tetrafluoroborate (^{18}F -TFB) via Radiofluorination of Boron Trifluoride and Evaluation in a Murine C6-Glioma Tumor Model. *Journal of Nuclear Medicine*, 2016, (suppl) S2721a.
- 5) DeGrado T, Kemp B, Pandey M, Jiang H, et.al. First-in-human PET Imaging of ^{63}Zn -zinc Citrate in Healthy Elderly Subjects and Patients with Alzheimer's Disease. *Journal of Nuclear Medicine*, 2016, (supp) S127
- 6) Jiang H, Pandey M, DeGrado T. Synthesis of [F-18] Tetrafluoroborate via Radiofluorination of BF_3 . *Journal of Labelled Compound and Radiopharmaceuticals*, 2015, (suppl) S255.
- 7) DeGrado T, Nathan G, Jiang H, et.al. Automated Production of F-18-labeled Acyl Fluorides as F-18-fluorination Synthons. *Journal of Labelled Compound and Radiopharmaceuticals*, 2015, (suppl) S200.
- 8) Pandey M, Jiang H, et.al. Cyclotron Production of ^{68}Ga Using a Solution Target. *Journal of Nuclear Medicine*, 2014, (supp) S434.

Patents

- 1) Gaseous F-18 technologies. WO 2015/143019, PCT/US2015/021215
 - 2) High specific activity preparation of F-18 tetrafluoroborate. WO2017189415, PCT/US2017/029089
-

Song, Taehoon

From: Rakowski, Joseph <rakowski@karmanos.org>
Sent: Thursday, March 25, 2021 3:11 PM
To: Parker, Bryan
Subject: [External_Sender] RE: Karmanos Cyclotron Request
Attachments: Karmanos_Cyclotron_RSO_AU_Request_Revised.pdf

Revision attached.

From: Parker, Bryan <Bryan.Parker@nrc.gov>
Sent: Thursday, March 25, 2021 3:03 PM
To: Rakowski, Joseph <rakowski@karmanos.org>
Subject: [EXTERNAL] RE: Karmanos Cyclotron Request

This Message originated outside your organization.

Thank you for info, Joe. That helps immensely.

Could you please provide one last bit of info re: Dr. Jiang's experience? Please further clarify the typical amounts and types of "hands-on" experience with the various PET isotopes.

If you have any questions, please let me know.

Thanks.
Bryan

Bryan A. Parker
Senior Health Physicist
USNRC Region III
bryan.parker@nrc.gov
678-828-7050
630-515-1078 (fax)



From: Rakowski, Joseph <rakowski@karmanos.org>
Sent: Thursday, March 25, 2021 2:37 PM
To: Parker, Bryan <Bryan.Parker@nrc.gov>
Subject: [External_Sender] Karmanos Cyclotron Request

Documents attached. Thank you.

Joe Rakowski
(313) 576-9616

McLaren confidentiality statement: "The information contained in this communication, including attachments, is confidential, may be privileged, and is intended only for the use of the named recipient(s). Unauthorized use, disclosure, forwarding or copying is strictly prohibited and may be unlawful. If you have received this communication in error, please notify me IMMEDIATELY at the phone number or pager listed above."