



Saskatchewan Cyclotron Facility

Activity & Achievement Report

April 2023- March 2024



fedorukcentre.ca

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OPENING REMARKS



Message from the Executive Director

Dr. John Root,
Executive Director
Fedoruk Centre

During the reporting period ending in March 2024, the Saskatchewan Cyclotron Facility (Facility) produced and delivered FDG daily to Royal University Hospital (RUH), enabling a record number of PET-CT scans for cancer diagnosis. Clinical demand for FDG has increased steadily in recent years, creating high expectations for quality and reliability of supply from the Facility.

Academic teams continued to access the Facility and its workstations, generating new knowledge across areas such as cancer therapeutics, neurodegenerative diseases, animal health and plant sciences. Thirty-five young researchers were trained in safe radiological practices in the

Facility and held personal dosimeters for working in the Innovation Wing. Private-sector clients also accessed the Facility to produce high-demand radioisotopes, such as ^{67}Cu and ^{225}Ac , which are essential to develop next-generation cancer therapies.

One of the most visible examples of our team's impact came during the 11th International Conference on Isotopes (11ICI), a prestigious event that brought a global audience in nuclear science, medicine and technology to Saskatoon and our Facility. Staff played a central role in supporting Facility tours and showcasing the daily work that takes place here.

As Executive Director of the Fedoruk Centre, I am proud of the Facility team's contributions this year. Their dedication continues to strengthen Saskatchewan's capacity for nuclear innovation and reinforces our reputation as a centre of excellence in radiopharmaceutical production and applied nuclear research.



Message from the Facility General Manager

Dale Schick-Martin,
Saskatchewan Cyclotron
Facility General Manager

Eight years after initial commissioning, the Facility has matured into a resilient resource for the province and the country.

During the reporting period, the Facility provided services to public institutions in British Columbia, Alberta, Saskatchewan, Manitoba and Ontario as well as private companies in Saskatchewan and Ontario. We maintained master supply agreements for delivery of FDG to hospitals in Saskatchewan (414 deliveries),

Alberta and Manitoba (37 deliveries), as well as for the Western College of Veterinary Medicine (18 deliveries). In Saskatchewan, FDG from the Facility supported PET-CT scans in 3,333 cancer patients during the year.

The Facility also manufactured radioisotope and radiochemical products for researchers, including FDG, $^{11}\text{CO}_2$, and ^{89}Zr -oxalate. Other isotopes were received and handled safely for researchers under the Facility license: ^{65}Zn , ^{67}Cu , $^{68}\text{Ge}/^{68}\text{Ga}$, ^{161}Tb , ^{177}Lu , ^{203}Pb and ^{225}Ac .

Our Facility workstations include a wide range of specialized equipment, all accessible through user-access agreements. Working more closely with the USask Safety Resources group has allowed us to streamline user access and harmonize our safety program for many of our users.

Many thanks to the Fedoruk Centre team, whose enthusiasm and cohesion are helping to build a reputation for the Facility as a client-focused resource.

The Saskatchewan Cyclotron Facility is Saskatchewan's sole producer of FDG (fluorodeoxyglucose), a radiopharmaceutical used in nuclear imaging to detect cancer.

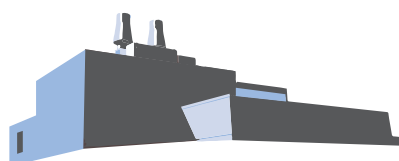
FACILITY BASICS

About the Saskatchewan Cyclotron Facility (Facility)

The Facility is operated by the Sylvia Fedoruk Canadian Centre for Nuclear Innovation Inc. (Fedoruk Centre) under an operating license with the University of Saskatchewan (USask).

Since beginning operations in 2015, the Facility has been maintained in a competitive state of readiness for access by academic and industrial researchers for the production of radiopharmaceuticals that are needed in medical imaging at regional hospitals.

TIMELINE



2015

The Saskatchewan Cyclotron Facility opened on the USask campus, with The Facility assuming operational responsibility.

2016

The first cancer patient was scanned at RUH using FDG produced at the Facility.



Fluorodeoxyglucose (¹⁸F)

\$4.2M



2020

A \$4.2M renovation to the Facility was completed in March 2020 with the opening of the Innovation Wing to meet growing research and industry needs.

2023

The Facility surpassed its previous achievement of supporting over 2,500 annual patient scans at RUH by providing enough batches of FDG to RUH to support over 3,000 patient scans*.

**See Chart 1 on page 15*

**OVER
3000
SCANS**



FACILITY USER INNOVATIONS

User Access

The Fedoruk Centre offers access for researchers and students from academia and industry to advance their programs of innovation in nuclear imaging and therapies or life sciences at Facility workstations. Workstation access is arranged through a user-agreement and preparatory discussions described on our webpage on cyclotron lab services: fedorukcentre.ca/our-offering/cyclotron-lab-services.php

For research in the public domain, rates for workstation access are set to recover the full cost of Facility operation if a single user occupied all workstations full-time. Rates are increased, to recover the full cost of operating the entire Fedoruk Centre (including Project funding and Program partnership investments) if a single user occupied all workstations full-time for proprietary research. This pricing rationale respects the principles that taxpayer funds are not applied to the benefit of individuals or single companies outside a fair and open decision-making process, and that the Fedoruk Centre is a not-for-profit corporation, delivering societal and economic benefits to Saskatchewan as a whole.

During the reporting period, the Fedoruk Centre and USask executed five new agreements for



Fedoruk Centre staff assist academic and industry researchers, providing the technical support needed to advance their work in cancer therapeutics, neurodegenerative diseases, animal care and plant science.

academic user access to Facility capabilities. One user access agreement was executed with industry clients for proprietary research. Actual Facility access during the reporting period enabled 11 individual research leaders and their teams to occupy Facility workstations for about 7,500 hours total.

Trends of user access to the Facility to advance their research programs are presented in Table 1. During the reporting period, eight tour events were held at the Facility for stakeholders, delegates, potential clients and interested members of the public, including conference attendees at the 11ICI conference, which was managed by the Fedoruk Centre as a service to the World Council on Isotopes.

Table 1 – Users Accessing the Facility to Perform Research

User Type	Fiscal Year Ending March 31				
	2020	2021	2022	2023	2024
Industry Researchers	5	3	6	12	5
Faculty Researchers	10	4	3	2	2
Post-doctoral Research Associates	20	10	14	8	8
Graduate Students	18	11	18	22	23

User-Driven Research

Ankon Das, a member of Gurpreet Aulakh's research team, prepares equipment inside a biosafety cabinet.



Actual Facility access during the reporting period enabled 11 individual research leaders and their teams to occupy Facility workstations for about 7,500 hours total.

In Table 2 below, examples are listed to illustrate the public-domain research that was led by USask scientists with support from the Facility.

Table 2 – Examples of Research Led by USask Scientists During the Reporting Period

Project Title or Description	Project Leader
Development of new diagnostic agents for lung inflammation imaging procedure	Aulakh
Development of nuclear imaging tools for pre-clinical evaluation of lung inflammation	Aulakh
Development of novel radioimmunotherapies for the treatment of invasive fungal infections	Dadachova
Radiolabelled imaging agents for cancer in mouse models	Fonge
Development of new capabilities for manufacturing cold-kits drug	Fonge
Radiochemical method development towards next-generation radiopharmaceuticals using radiometals and radiofluorine	Price
Multi-centre development of radionuclides	Price
Detecting responses to anti-cancer therapies	Geyer
3'- ¹⁸ F-ABA: a PET probe to image ABA transport in plants	Phenix
Towards radiotracers for GCase	Phenix
Synthesis of fluorinated cannabinoid derivatives	Phenix
¹¹ C-Acetate synthesis	Siciliano
Targeted radionuclide therapy (TRT)	Geyer
Production of [⁶⁸ Ga]Ga-PSMA	Fonge
Radioimmunotherapy for cancer and multiple sclerosis	Dadachova
Intranasal administration of [¹⁸ F]FDG or [¹⁸ F]FLT	Geyer
[¹⁸ F]F(aq) / [¹⁸ F]-FDG soil core dosing and imaging	Siciliano
Synthesis of ¹⁸ F-labelled benzene and toluene and soil imaging	Siciliano
Use of PET for imaging of root N ₂ fixation	Hallin

HIGHLIGHTS OF USER RESEARCH AND DEVELOPMENT



Medical Imaging and Plant Science at the Saskatchewan Cyclotron Facility

With support from the Facility, USask researchers Dr. Chris Phenix (PhD) and Dr. Sue Abrams (PhD), developed a novel method to study how plants respond to environmental stress using radiotracers typically applied to human health. The team tagged the plant hormone abscisic acid (ABA) with fluorine-18 (^{18}F) to study how and where a plant's stress response is triggered.

By combining expertise in radiochemistry and plant biochemistry, the teams were able to visualize how ABA moves through a plant under

conditions such as drought, frost or disease. PET imaging and the availability of radioisotopes was available thanks to Phenix's research funding and access to the Facility.

The research revealed that plants, like humans, transmit internal signals in response to stress, and that these signals can be tracked using advanced imaging tools. This work not only offers new insights into how plants adapt to challenging environments, but also highlights the potential of nuclear imaging technologies to acquire new knowledge advancing climate-resilient agriculture.

The team's interdisciplinary approach demonstrates how nuclear-based imaging science can support research beyond health care. Moving forward, they plan to apply their method to explore how plants respond to other stressors.



Comparative Oncology in Action

Dr. Behzad Toosi (PhD), assistant professor with USask's Western College of Veterinary Medicine (WCVN), and his collaborators from across USask, including in chemistry and medicine, are using tools available through the Fedoruk Centre to test new cancer therapies in companion animals.

His work focuses on comparative oncology, a field that explores how research on naturally occurring cancer in pets like dogs and cats can help speed up the development of new cancer treatments for humans.

The Facility provides access to radioisotopes used in micro-PET-CT imaging and space for working with live specimens. This support helps the research team to radiolabel new compounds and monitor how they work inside the body if they are used for cancer diagnosis and/or treatment

purposes. This includes how they're absorbed, where they go and how effective they are over time.

One current project involves a novel specific antibody developed by a private-industry partner, Biomirex Inc. Early results for using this antibody in humans has been promising, and the team is now working to adapt this antibody for safe use in diagnosing cancer at early stages and for the treatment of cancer in companion animals. Using the Facility's imaging tools, they hope to track the antibody's safety and effectiveness in dogs and cats before moving further into clinical trials.

Toosi says the research wouldn't be possible without the shared expertise and equipment available at USask and through the Fedoruk Centre. He sees this kind of interdisciplinary collaboration as critical to the success and progress of cancer therapy.

"We've been privileged to have support of the Fedoruk Centre and our university," said Toosi. "By nurturing our collaborative and collective efforts on campus, we empower each other and the team and our university community to achieve significant milestones that could revolutionize cancer therapy."



Supporting ^{67}Cu Cancer Therapy Development with Iotron Medical Inc.

Near the end of the reporting period, the Fedoruk Centre entered into an agreement with Iotron Medical Inc., an entrepreneurial company aiming to become the world's leading supplier of the medical isotope ^{67}Cu . ^{67}Cu is a promising isotope for targeted cancer therapy, offering both imaging and therapeutic benefits in a single agent.

Under this agreement, Fedoruk Centre staff at the Facility provide processing space and technical support to help purify ^{67}Cu material produced at the Canadian Light Source (CLS). Staff at the



Iotron Medical Chief Executive Officer and President, Patrick Donahue

CLS use a linear accelerator to produce ^{67}Cu , which is then transported to the Facility, where it is separated and purified into $^{67}\text{CuCl}_2$ —an active pharmaceutical ingredient ready for delivery to Iotron clients.

The availability of the Facility's world-class equipment and highly trained staff is critical to Iotron's ability to deliver purified ^{67}Cu for clinical and research use.

This collaboration represents an important step in expanding access to isotopes used in developing next-generation cancer treatments and provides Fedoruk Centre staff with the opportunity to support new products for international use.



Iotron research lab

CAPABILITY AND PERFORMANCE

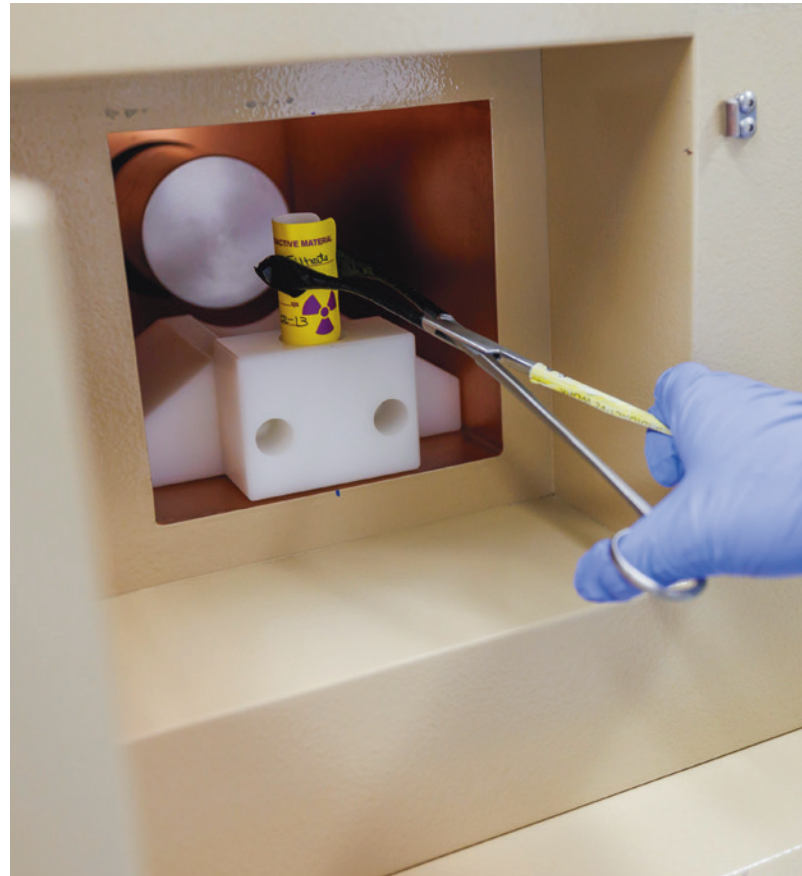
Infrastructure Upgrades

The Facility fully validated a new sterility and environmental monitoring laboratory to bring sterility testing in-house. Going forward, the Fedoruk Centre will maintain its own system for validated sterility tests in a laboratory that complies with Health Canada's requirements for Good Manufacturing Practice (GMP). This will improve the reliability of sterility testing by removing uncertainty and timing challenges imposed by sending samples to a third-party laboratory.


The TR-24 cyclotron had a prototype circulator removed from service to realign its radiofrequency (RF) system with other ACSI cyclotrons. This retrofit will ensure RF functionality is more comparable to other existing cyclotrons, and the data generated by the circulator will support ACSI's development of a solid-state RF system.

Products and Trends

The isotope ^{89}Zr has been produced at the Facility and supplied to users sporadically for over three years. The capability has allowed the Fedoruk Centre to participate in a Collaborative Research Project (CRP) with the International Atomic Energy Agency (IAEA), and work with leading ^{89}Zr producers from around the world. The meeting was scheduled for April, 2024 with the Fedoruk Centre as the sole representative of Canadian ^{89}Zr innovation in attendance.



On January 13, 2023, the Fedoruk Centre secured a contribution of \$410,650 for *Commercializing Capabilities at the Saskatchewan Cyclotron Facility* from the Regional Innovation Ecosystems (RIE) program of Prairies Economic Development Canada (Prairies Canada). As part of this project, development of three products commenced during the reporting period: $^{68}\text{GaCl}_3$, Na^{18}F , and ^{18}F -PSMA. Na^{18}F became available to users as of August. The production process of $^{68}\text{GaCl}_3$ was successfully validated and on-request orders are now available. The radioisotope ^{18}F -PSMA is in a planning phase, with project materials purchased through early 2024.

A photograph of a male staff member with a beard and glasses, wearing a blue lab coat and white gloves, working in a laboratory. He is seated at a desk with a laptop, looking towards the camera. In the background, another staff member is working with a large piece of equipment featuring multiple robotic arms. The lab coat has a 'Fedoruk Centre' logo and the name 'Kalum' on it. A name tag is also visible.

A Fedoruk Centre staff member is assembling a TRASIS® auto synthesizer cassette for purifying Zirconium-89 radiometal.

Fedoruk Centre staff at the Facility regularly include work on internal projects to produce and chemically isolate radioactive isotopes with the goal of expanding the availability of isotopes for researchers and clients.

Table 3 – Trends of Facility operational performance indicators

Performance Indicator	Fiscal Year Ending March 31				
	2020	2021	2022	2023	2024
Workstation availability – ready for user access (percentage of total time)	90.3%	95.8%	97.0%	98.2%	96.2%
Workstation occupancy by users (percentage of available time)	36.1%	14.7%	15.3%	13.2%	11.8%
Unplanned outages of cyclotron (days)	9	4	5	4	10
Unplanned outages of Facility production (days)	9	5	6	6	12



Fedoruk Centre Operation Technologists at work on the cyclotron power system, ensuring reliable performance for isotope production.



Fedoruk Centre Production Technologist using robotic arms in the hot cell room during the manufacture of FDG, a radiopharmaceutical produced daily for clinical PET-CT imaging.

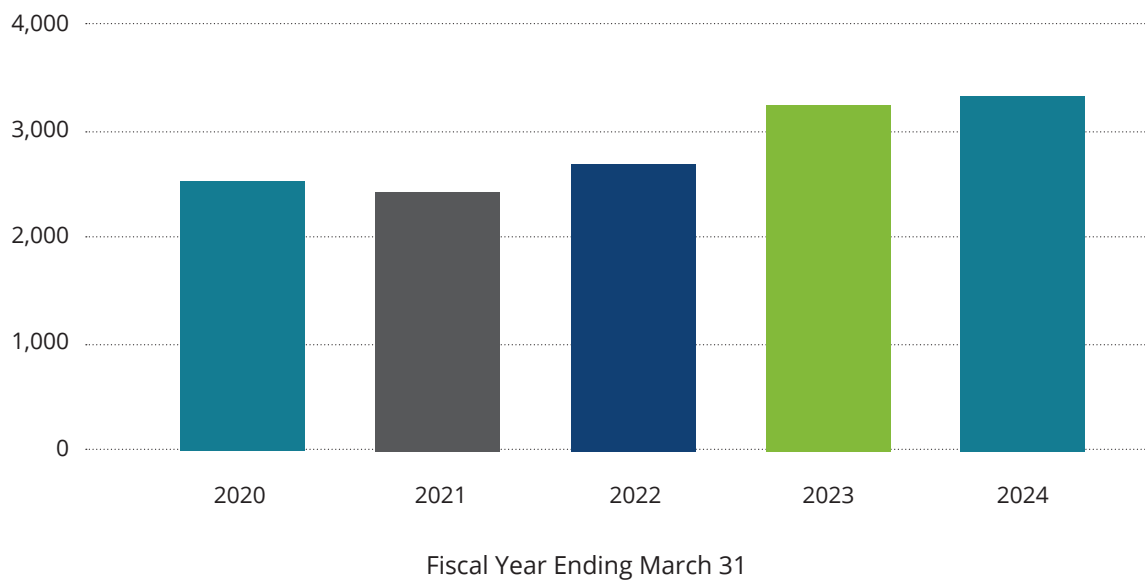
Production of FDG and Other Isotopes

The Facility manufactures the nuclear imaging agent FDG for daily delivery to the PET-CT scanner at the RUH in Saskatoon. Typically, production begins at 4:00 am each morning with proton-irradiation of an ^{18}O -enriched water target, to generate the positron-emitting isotope ^{18}F , followed by chemical processing and testing for quality control. Delivery of FDG is made to the RUH by 8:00 am for patient diagnoses.

During the reporting period, the Facility team made 414 FDG deliveries to the RUH. This included 28 extra-delivery days scheduled to reduce the PET-scan patient waitlist. The Facility also provided 18 deliveries of FDG to the Western College of Veterinary Medicine and 37 batches of FDG to hospitals in Alberta and Manitoba. The number of PET-CT scans received by patients at the RUH with FDG produced at the Facility is pictured in Chart 1.

Number of PET-CT scans at RUH

Chart 1 – Number of patient PET-CT scans at RUH with FDG produced by the Facility



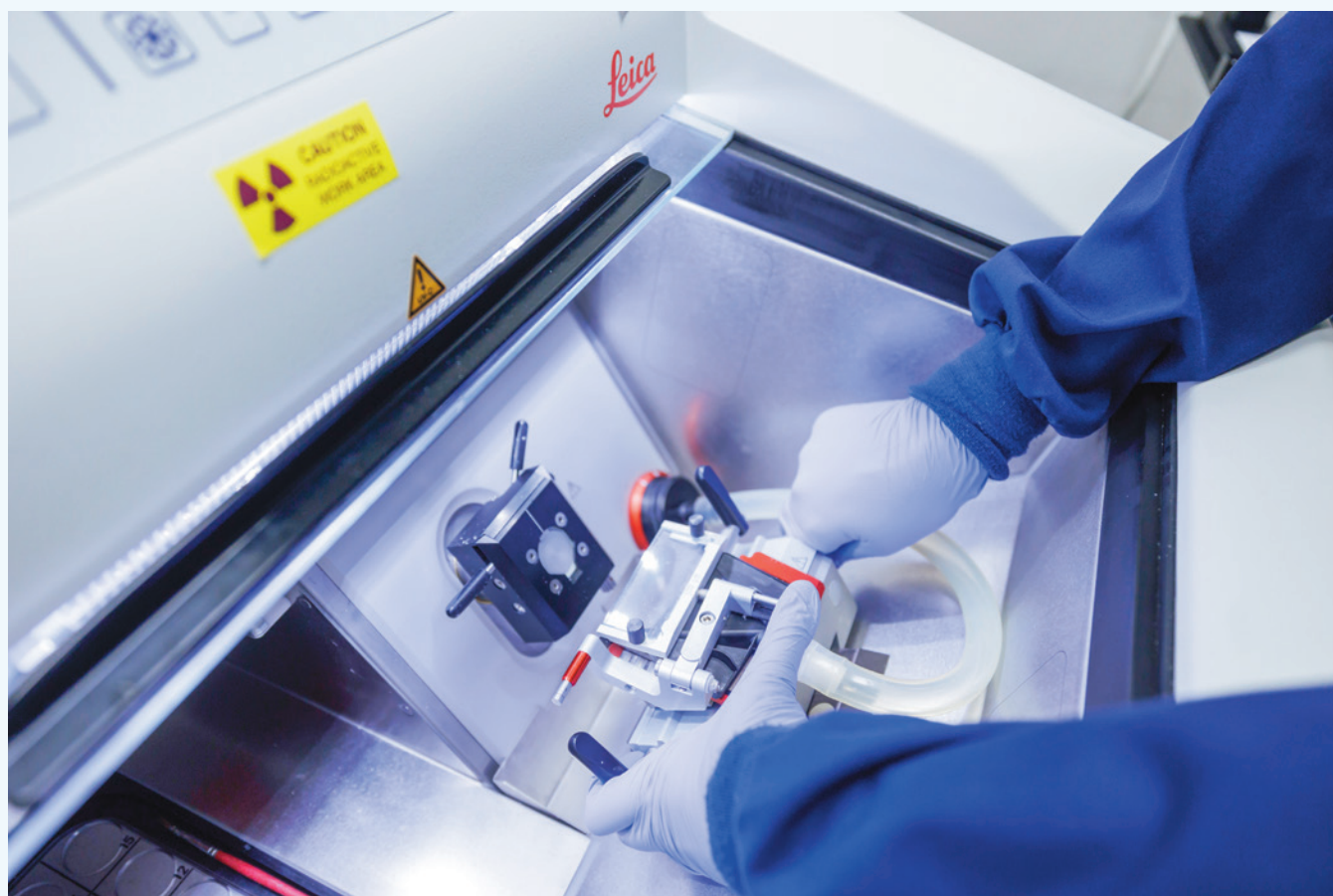
Additional radioisotopes were produced at the Facility for researchers, including ^{11}C , ^{13}N , ^{18}F and ^{89}Zr . A summary and multi-year comparison of isotope production for research is presented in Table 4.

Table 4 – Number of Isotope Batches Produced at the Facility for Researchers

Isotope	Calendar Year				
	2019	2020	2021	2022	2023
^{11}C	45	25	41	74	21
^{13}N	0	0	3	0*	0*
^{18}F	101	42	83	161	131
^{64}Cu	12	10	0	0	0
^{89}Zr	28	31	29	11	18
^{68}Ga	0	0	3	0	1

*Some ^{11}C productions were performed with the intention of using the co-produced ^{13}N

Several other isotopes were received and handled safely for researchers under the Facility license, including: ^{65}Zn , ^{67}Cu , ^{68}Ga (from a generator), ^{161}Tb , ^{177}Lu , ^{203}Pb and ^{225}Ac .



SAFETY

Licensing and Compliance

The Facility includes a TR-24 Cyclotron, labs for the safe handling of nuclear substances, equipment to manufacture and qualify radiopharmaceuticals for clinical applications in humans, and capacity to hold living specimens for preclinical research and other life sciences. These activities are regulated under the authorities of the Canadian Nuclear Safety Commission (CNSC), Health Canada (HC), the Public Health Agency of Canada (PHAC) and USask, with key licenses and permits being:

- CNSC Class II Facility and prescribed equipment License;
- CNSC Nuclear Substances and Radiation Devices (NSRD) License;
- HC Drug Establishment License (DEL);
- USask Biosafety Permit.

The Fedoruk Centre professional and technical staff work together to ensure compliance with terms of all these permits, and comply also with the Canada Labour Code, and guidelines of the Canadian Council on Animal Care. We appreciate the cooperation of our users in helping us ensure the Facility is a safe, respectful workplace, compliant with the requirements of our licensing authorities. Some notable areas of growth include:

- As of November 1st, the Fedoruk Centre entered an agreement with Safety Resources at USask to have 1.0 FTE equivalent of Safety Resources' time supporting the Fedoruk Centre's radiation, biological, laboratory and workplace safety programs.
- During the reporting period, the Fedoruk Centre Class II license was amended to allow handling of all radioisotopes up to atomic number 82 (Pb) in quantities up to 37 GBq. This allows much greater flexibility for starting up experiments with novel isotopes.
- Over the calendar year 2023, no staff at the Facility received even 10% of the regulatory whole-body exposure limit (50mSv) for the year.



Radiation and Safety Training

Our radiation protection program guides all the safety protocols at the Facility. The program includes an Occupational Health and Safety Committee that meets quarterly and biannual Facility inspections.

Staff and users are trained and qualified as Nuclear Energy Workers (NEWs). Everyone is

expected to conduct their work in a manner to ensure radiation exposures are below the administrative limits established through the Radiation Protection Program, respecting the principle of ALARA (As Low As Reasonably Achievable) and well under CNSC regulatory limits for all Nuclear Energy Workers.

"Everyone at the Facility works hard to ensure that anyone who walks through our doors is safe. We meet all regulatory standards and undergo regular training to go above and beyond what's expected of our team."

– Fedoruk Centre staff member



A research team member uses a hand-held monitoring tool to check radiation levels, ensuring a safe working environment during isotope use.

PUBLICATIONS ARISING FROM FACILITY ACCESS

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 Inorg. Chem. **63**(50): 20806-20819 (2023)
 DOI: 10.1021/acs.inorgchem.2c03573
- A Systematic Investigation into the Influence of Net Charge on the Biological Distribution of Radiometalated Peptides Using [⁶⁸Ga]Ga-DOTA-TATE Derivatives**
 Shvan J. Raheem, Akam K. Salih, Moralba Dominguez Garcia, Jessica C. Sharpe, Behzad M. Toosi, and Eric W. Price
 Bioconjugate Chemistry **34** (3): 549-561 (2023)
 DOI: 10.1021/acs.bioconjchem.3c00007
- A Theranostic Approach to Imaging and Treating Melanoma with ²⁰³Pb/²¹²Pb-Labeled Antibody Targeting Melanin**
 Jiao, R., Allen, K.J.H., Malo, M.E., Yilmaz, O., Wilson, J., Nelson, B.J.B., Wuest, F., Dadachova, E.
 Cancers **15**: 3856-61 (2023)
- CD34 Protein: Its Expression and Function in Inflammation**
 Carolina Rego Rodrigues, Sahib Moga, Baljit Singh, Gurpreet Kaur Aulakh
 Cell and Tissue Research **393**: 443-454 (2023)
<https://doi.org/10.1007/s00441-023-03811-4>
- Characterization of IGF2R Molecular Expression in Canine Osteosarcoma as Part of a Novel Comparative Oncology Approach**
 Boisclair C, Dickinson R, Giri S, Dadachova E, MacDonald-Dickinson V.
 Int J Mol Sci. **24**(3): 1867 (2023)
- Comparative Molecular Characterization and Pharmacokinetics of IgG1-Fc and Engineered Fc Human Antibody Variants to Insulin Growth Factor Receptor Type 2 (IGF2R)**
 Prabakaran, C.B.; Giri, S.; Allen, K.J.H.; Bato, K.E.M.; Mercado, T.R.; Malo, M.E.; Carvalho, J.L.C.; Dadachova, E.; Uppalapati, M.
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- Development and Biodistribution of a Nerve Growth Factor Radioactive Conjugate for PET Imaging**
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 Molecular Imaging and Biology January 2023
<https://doi.org/10.1007/s11307-023-01805-w>
- Evaluating the Targeting of a *Staphylococcus aureus*-Infected Implant with a Radiolabeled Antibody In Vivo**
 van Dijk B, Hooning van Duyvenbode JFF, de Vor L, Nurmohamed FRHA, Lam MGEH, Poot AJ, Ramakers RM, Koustoulidou S, Beekman FJ, van Strijp J, Rooijackers SHM, Dadachova E, Vogely HC, Weinans H, van der Wal BCH.
 Int J Mol Sci. **24**(5): 4374 (2023)
- Expression of Pentraxin 3 in Equine Lungs and Neutrophils**
 Michelle Townsend, Brooke Fowler, Gurpreet K. Aulakh, Baljit Singh
 The Canadian Journal of Veterinary Research **87**: 9-16 (2023)
- Image-Based Dosimetry in Dogs and Cross-Reactivity with Human Tissues of IGF2R-Targeting Human Antibody**
 Allen KJH, Kwon O, Hutcheson MR, Grudzinski JJ, Cain SM, Cruz FA, Vinayakamoorthy RM, Sun YS, Fairley L, Prabakaran CB, Dickinson R, MacDonald-Dickinson V, Uppalapati M, Bednarz BP, Dadachova E.
 Pharmaceuticals (Basel) **16**(7): 979-984 (2023)

PUBLICATIONS ARISING FROM FACILITY ACCESS

11. **Modulation of Low-Dose Ozone and LPS Exposed Acute Mouse Lung Inflammation by IF1 Mediated ATP Hydrolysis Inhibitor, BTB06584**
 Pahul Singh, Gurpreet Kaur Aulakh
 Front. Immunol. **14**: 2023
 Sec. Cytokines and Soluble Mediators in Immunity
<https://www.frontiersin.org/articles/10.3389/fimmu.2023.1126574/full>
12. **Radiochemical, Computational, and Spectroscopic Evaluation of High-Denticity Desferrioxamine Derivatives DFO2 and DFO2p toward an Ideal Zirconium-89 Chelate Platform**
 Elaheh Khozeimeh Sarbisheh, Kelly L. Summers, Akam K. Salih, Julien J. H. Cotelesage, Amanda Zimmerling, Ingrid J. Pickering, Graham N. George, and Eric W. Price
 Inorganic Chemistry **62**(6): 2637-2651 (2023)
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13. **Radioimmunotherapy for the Treatment of Infectious Diseases: A Comprehensive Update**
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14. **Radioimmunotherapy as a Pathogen-agnostic Treatment Method for Opportunistic Mucormycosis Infections**
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 DOI: 10.1099/acmi.0.000671.v4
15. **Targeted Radionuclide Therapy of Cancer and Infections**
 van der Wal BCH, Dadachova E.
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 J Nucl Med **64** (11): 1676-1682 (2023)
 DOI: 10.2967/jnumed.123.265906

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