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CERN-MEDICIS: OPERATIONAL INDICATORS TO SUPPORT THE PRODUCTION OF NEW MEDICAL RADIONUCLIDES BY MASS SEPARATION*

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Abstract

CERN-MEDICIS is an isotope mass separation facility dedicated to biomedical research located in a type A work sector, receiving on average 50% of the 1.4 GeV protons delivered by the Proton Synchrotron Booster (PSB). It was commissioned with Radioactive Ion Beams (RIB's) in 2017. MEDICIS has operated for the past 5 years in batch mode, with targets irradiated in a station located at the HRS beam dump, and with external sources provided by MEDICIS cyclotrons and nuclear reactors partners, notably during the Long Shutdown (LS2). Additional features of the facility include the MELISSA laser ion source, radiochemistry on implanted radionuclides and an online gamma-ray spectroscopy implantation monitoring. In 2022, we introduced Key Performance Indicators (KPI's) to monitor the operation of the facility for collected efficiencies, the optimization of the radiological risks and evaluate impact of possible modifications of the station, paralleling for instance LHC's integrated luminosity. Defined KPI's cover aspects in the operation cycle, e.g. planning in CERN schedule, target irradiations, duration of the process, radiological risk mitigation, facility uptime, developments and maintenance. MEDICIS KPI's can help distinguish which of the operation and infrastructure life cycle requires immediate intervention, developments or consolidation. Those are related to the irradiation stations and irradiation possibilities, the beam-lines (parallel collections), target and ion sources (reliability), robot handling and infrastructure, or the separation process itself.

INTRODUCTION

CERN-MEDICIS is an isotope mass separation facility located in a type A work sector laboratory according to the Swiss legislation on Radiation Protection [1] that produces batches of non-conventional radionuclides and purity grades, for research performed at biomedical institutes to develop new imaging and therapeutic radiopharmaceuticals [2]. The production of the radionuclides follows the following sequence [3]:

1- target irradiation at CERN on stations located between the ISOLDE targets and beam dumps, or reception of targets irradiated at cyclotrons or reactors;
2- performing isotope mass separation by target heating to high temperatures (>2000 °C), production of an isotope secondary beam with a 1^+ ion source, steering and mass separation through a double focusing dipole magnet;
3- implantation of the ions into salt or metal backed-foils in a dedicated vacuum chamber;
4- radiochemical purification (when required) and characterization before dispatch to partner institutes where radionuclides are used for biomedical research projects.

The review of the performance of accelerators and facilities has been a long tradition in accelerator facilities, and at CERN itself with e.g. the launch of the Chamonix workshops series in 1991, where the performance of the LEP was discussed at the time, and later of the LHC and the full accelerator complex, associated with elements of consolidation and technical infrastructure upgrades [4]. On the other end, it has to be noted that facilities exploiting cyclotrons and nuclear reactors delivering radionuclides, may use another set of parameters to evaluate their performances.

When dealing with radionuclide production for medical applications, the required processing and logistics time from production to dispatch leads to the definition as operational indicator of a 6-days Curie equivalent for Mo-99 (main radionuclide in nuclear imaging), that corresponds to the activity remaining after 6 days of decay [5].

When dealing with a facility producing RIBs like ISOLDE, we for instance included the following figures of merit to elaborate on the advantage to upgrade the PSB proton beam energy from 1.4 to 2 GeV made possible by the LIU/HiLumi HL-LHC upgrade projects at CERN [6, 7]:

- Yields;
- Beam purity;
- Availability of the facility (uptime);
- Number of different RIBs

Some of these figures of merit, e.g. the radioactive ion beam yield, when folded with the number of protons on target (PoT), will match the integrated luminosity that are

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often introduced in particle colliders. The facility uptime is often taken as reference, and the Accelerator Fault Tracking system (AFT) had been developed for CERN accelerators [8]. Other KPI used at CERN is for instance the electrical consumption of an accelerator, GWh.fb-1 as followed by the CERN energy panel [9].

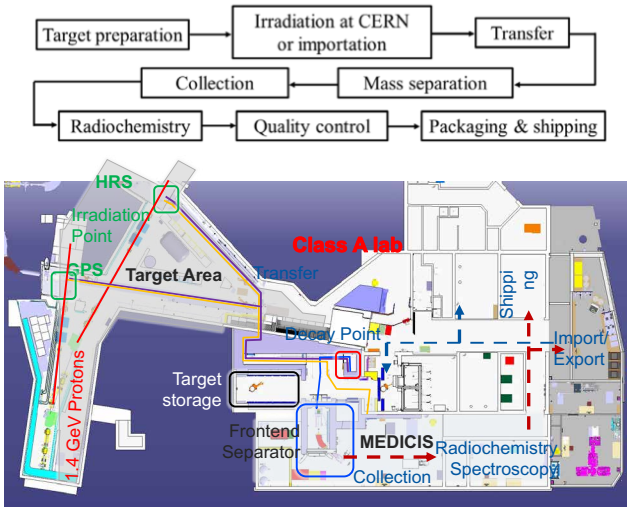

Figure 1: MEDICIS operation steps (top); corresponding layout (bottom).

CERN-MEDICIS FACILITY AND PROCESS

The sequence of operation required from the production of the radionuclides to the shipping to the research laboratory part of the MEDICIS collaboration involves different interfaces and groups, notably CERN Groups across departments, institutes importing/exporting radionuclides, local and national authorities, as well as external companies authorized to proceed with class 7 radioactive transport and custom clearance. The organisation and proper planning is therefore of prime importance, because intrinsically the time required to perform the full process from door to door will automatically translate into reduced activities following the well-known nuclear decay law [3]. The half-life of radionuclides produced at MEDICIS range from a few hours to a few days, with two extremes, that of C-11 production for the development of a target material for the production of hadron-therapy beams ($T_{1/2}$ = 20.4 min) and of Ac-227 ($T_{1/2}$ = 21.6 years) collected for the investigation of dosimetric impact when found as impurities in Ac-225 collections [10, 11].

The planning of the full process, its coordination, and finally possible deviations will ultimately impact on the full extent of the different operational steps, and its associated radionuclide decay (Fig. 1) [5, 12].

The target irradiation, the subsequent mass separation and collection process represents a core expertise of the MEDICIS facility with advanced target and ion source designs, beamline operation, and collection monitoring. Recent reviews have been made on the MEDICIS isotope separation process, notably describing how an increased collection efficiency was achieved or how sputtering effects were taking place [3].

KEY PERFORMANCE INDICATORS FOR MEDICIS

The introduction of Key Performance Indicators to monitor and provide feedback on the yearly operation of the facility was introduced after an operation review held in 2022 [13].

KPI#1: Collection Efficiency and Collected Activity (0-100% / kBq-GBq)

This first KPI reflects the overall performance of the separation process, efficiency, and the associated collected activity. Maximizing both figures allows to more efficiently exploit the infrastructures. In Fig. 2, we display KPI#1 for Sm-153 over 2020-2022 and provide a focus on Ba-128 collections performed by target irradiations in 2022 (bottom figure). While activities and efficiencies at the End of Collection (EoC) can be precisely assessed for radionuclides received from outside institutes, where the activity and radionuclide inventories are reported (as an obligation from the transportation regulations), the radionuclide inventory in case of in-house irradiation of targets into which occurs spallation reactions is difficult to measure and must be computed by numerical simulations. To improve the quality of the simulations., the scattered beam profile and position were measured with radiation sensitive GAFchromic™ films, which indeed identified differences in the position of the irradiation station. The beam position was corrected for the campaign of 2022, and the irradiation station modified for the starting campaign of 2023 to better capture the scattered PSB beam.

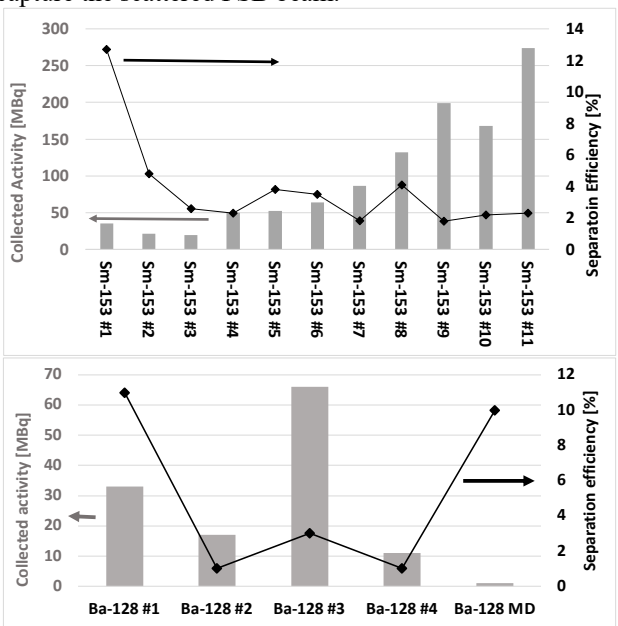

Figure 2: Bottom: KPI#1 computed for Ba-128 collections from Ta target irradiations in 2022. Activities (bars, left axis) are given for End of Collection (EoC). Top: Collections of Sm-153 over 2020-2022. Efficiencies (diamonds and lines, right axis).

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KPI#2: Dosimetry (μSv / # of Deviations)

The operation, handling and manipulation of unsealed radioactive samples, as those performed at MEDICIS, calls for dedicated infrastructures, trained operators (category A and B workers) and scientists, and proper monitoring and review performed by the HSE-RP Radioprotection group [14]. The operation follows the As Low As Reasonably Achievable (ALARA) optimization procedure, with risk analysis and mitigation measures whenever appropriate, use of protective equipments for the exposed staff, and evolution of the infrastructure with the procurement of local shielding and gloveboxes. KPI#2 should therefore be minimized and is reported for the handling of the different radionuclides that took place in 2022. For each operation, a work and dose planning (WDP) is elaborated, and optimized with dosimetry followed during and after operation [15]. From Table 1, while about 30 GBq in the form of unsealed radioactive samples were handled, it resulted in limited exposure to the MEDICIS staff as shown with the low reported figures.

Table 1: KPI#2: Dosimetry for Radionuclides Handled in 2022 (Total Dose).

Radionuclide	# of collections	Collective dose [person.μSv]	Max individual dose [μSv]	Events
Sm-153	2	3	2	-
Ba/Cs-128	6	6	3	-
Tm-165	1	0	0	-
Tm-165/167	1	5	3	-
Sc-44/47	2	0	0	-
Hg-195/197	1	9	4	-
Ac-225/227	1	0	0	-
Tb-155	4	76	19	-

If a deviation with significant radiological impact occurs, e.g. predicted dose exceeded by more than 50% or a contamination event, a dedicated follow-up is put in place.

KPI#3: Decay Loss (process, import/export vs isotope half-life) and KPI#4: Importance of Delivering

The two additional KPI's were introduced to address the optimization of the scheduled and realized separation processes on the one hand, and to identify collections which require deliveries on time and according to performance criteria, such as those required for biomedical research with protocols using animals, and those which may arise possibly in an hospital setting. These two KPI's reflect an optimized exploitation of the planning and organization of the operation with the different interfaces, where a low KPI#3 means that margin can be gained to reduce the radionuclide decay loss in the full operation chain, while KPI#4 reflects on different impacts that a radionuclide delivery may induce on the developed biomedical research projects. Figure 3 shows KPI#3 expressed as the fraction left after radioactive decay, at the end of the MEDICIS operational steps (Fig.1), together with the associated isotope half-life (continuous line, right axis). KPI#4 is set respectively to 1, 2 or 3 for routine, fair, and important collections. A target unit failure and a faulty extraction electrode mechanism resulted in KPI#3 set to 0. Most of the important deliveries in 2022, notably Ba-128 to CHUV Lausanne Hospital and Tb-155 to PSI had satisfactory operation process management (high KPI#3), with a notable exception for Sm-153 imported and re-exported to SCK CEN Belgium nuclear center with significant decay losses are reported for KPI#3.

CONCLUSION AND OUTLOOK

The last year of operation at MEDICIS has seen the introduction of KPI's to help identifying strengths and points of improvement. The overall dosimetric impact of the facility is very low, yet interesting performance is already achieved notably for Ba-128 and Sm-153 in 2022, two radionuclides that were already delivered to partner institutes that produced important results in biomedical research, now promoted in the PRISMAP European Medical Radionuclide Programme [16]. While already relevant activities are delivered for the separation process of Sm-153 for preclinical research, margins of progression can clearly be identified from KPI#2 and#3 for exploitation in clinical research.

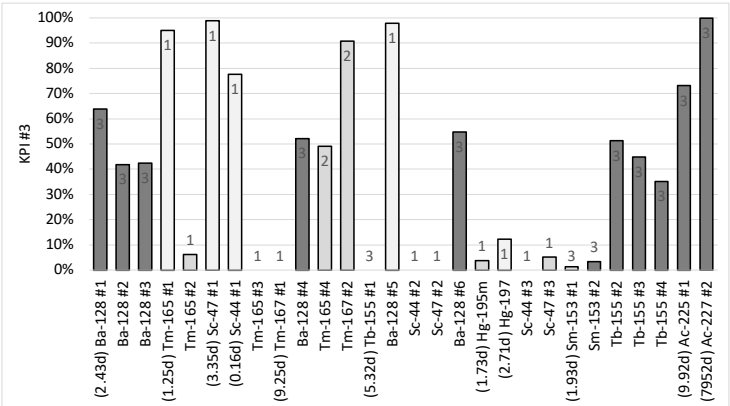

Figure 3: KPI#3 for collections performed in 2022; together with KPI#4 (3 in dark grey, 2 in grey, 1 light grey, see text). The corresponding radionuclide half-life is reported in bracket for each radionuclide.

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