European Organization for Nuclear Research
Organisation européenne pour la recherche nucléaire

CERN MEDICIS – 12th Collaboration Board meeting

CERN, 01 July 2024
Minutes by C. Duchemin, E. Mamis, T. Stora / DRAFT
Link to the agenda and MEDICIS proposals https://indico.cern.ch/event/1418414/
Link to the MEDICIS proposals: https://medicis.cern/approved-projects

Agenda:

Participants:
Charlotte Duchemin - CERN
Thierry Stora - CERN
Agata Rotzika - CERN
Alessandro Raimondo - CERN
Amedeo Habsburg - CERN
Antonio Paulo - IST
Edgars Mamis – CERN/U. Latvia
Frank Bruchertseifer - JRC
Frederic Bois - HUG
Jake Johnson – K U Leuven
Katarina Sigerud - CERN
Laura Lambert - CERN
Maija Radzina – U. Latvia
Marietta Straub – IRA-CHUV
Michael Lassmann – EANM
Muhammad Inzamam – CERN/PAEC
Nick Van der Meulen - PSI
Patricija Kalnina – U. Latvia
Peter Ivanov - NPL
John Prior - CHUV
Ruslan Cusnir – IRA-CHUV
Sean Collins - NPL
Simone Gilardoni - CERN
Toms Torins – U. Latvia
Valentina Garibotto - HUG

Thierry Stora opens the 12th Collaboration Board. Minutes of the 11th Board are approved.

MEDICIS Collaboration: different schemes of operation (MoU, Budget & Financial Report)
The financial report is introduced - See https://indico.cern.ch/event/1418414/contributions/5985352/attachments/2888483/5063005/MEDICIS%20Financial%20report_%20FY2023.pdf

Expenses for MEDICIS operation have been split between the MEDICIS Collaboration budget code and CERN budget code which is provided for the missing operation funds from the collaboration. In addition to material expenses, an equivalent staff position has been supported

from CERN in the HSE unit. Revenues were split from different members of the collaboration for a total of 212 kCHF. An additional revenue of 45kCHF was obtained through donations towards CERN&Society. Alessandro Raimondo then provided details on in-kind contributions. This is shared between equipment, secondment of experts and radionuclide sources provision.

Simone Gilardoni comments that this report is important for CERN's management, as we are requested to trigger external funding to complement CERN fundings.

To further elaborate on the link to EU support actions, Thierry Stora said that the agenda is made to first discuss the future of PRISMAP, as it has some non-negligible contribution to MEDICIS.

Future of PRISMAP: PRISMAP+

PRISMAP is an access infrastructure project that started 3 years ago on 01/05/2021. We are going through a review this Thursday with the Project Officer of the EU and an external expert. With the progress of PRISMAP towards this second review, we have very good news to report.
Radionuclides are not only made available by MEDICIS but from many other facilities taking part. Several call of projects were launched. The last one was completed end of 2023. During this last call of projects, there were several demands, in strong contrast with the call 3 where there was only 5 proposals and one granted. C. Duchemin is following up on the progress of the different projects.
As particular development highlights in the project:

- Tm-165 was delivered from CERN to DTU in 4 hours door-to-door with private jet. It was a first in the consortium as usually road transportation or plane carrier that is much slower and leading to non-negligible decay.
- A high power target development at GANIL for 10 kW, 40MeV alpha beam for At-211 production.
- Ra/Ac-225 was delivered by MEDICIS to NPL for a PRISMAP internal consortium project involving the university of Oslo.

PRISMAP most Key Performance Indicators (KPI's) have been met and some are even exceeded (see details in slide 4). A last call of project will be issued in the course of 2024.
There are two notable projects in PRISMAP aiming to perform first-in-human injections. P4 with Tb-161 in Italy. P31 involves MEDICIS with delivery of Pb-212 in Germany. Ra-224 was not in the initial list of radionuclides in PRISMAP but requested via the user community after its start.
These projects also justify the necessity of asking for an extension of PRISMAP.
The future of PRISMAP (PRISMAP+) is presented. An extension of 8 months of PRISMAP is requested to the EC with no additional budget. PRISMAP is included in the ERVI roadmap process lead by the European commission. PRISMAP+ has been identified and defined as project 4 (out of 6) .
A dedicated PRISMAP+ meeting will be organized in September in Nantes after the PRISMAP CM7. CERN will be coordinating and proposal is to keep SCIPROM to support the application.

Future of MEDICIS by Simone Gilardoni

There was discussions on how to find alternative financial scheme.
The extension of the next 5 years of MEDICIS will be discussed in September 2024. The proposal of PRISMAP+ is pending the decision of the future of MEDICIS at CERN. In the next couple of months, this extension will be managed with the director of accelerators, chairing the CERN Medical Application Steering Committee. In general, there is a very positive attitude of CERN management which is very interested to help and support the continuation of MEDICIS.
Simone added that the management is aware that the collaboration is actively looking for funding. An external review also advised that more industrial partnership should be investigated.

As concluding comments, Simone Gilardoni thanks the colleagues from the MEDICIS collaboration who provided inputs and presentation during at the international review meeting held last September 2023. MEDICIS was praised on the output considering the resources available. The collaboration, in summer, will need to reiterate the interest for MEDICIS on the long term (5 to 10 next years).

MEDICIS Technical Stop, Restart and Schedule in 2024

The presentation of C. Duchemin covered MEDICIS activities since the last collaboration board in Dec. 2023.

9 new targets were used, and 6 reused. A record activity of 3.8 GBq was collected, and 25 shippings, a record for a regular year of operation at MEDICIS. Radiological exposition was reduced, following ALARA principles.

During the technical stop, many activities took place along the MEDICIS infrastructures and operation, namely: Labview control software updates,Ventilation checks, Electrical work, Gas injection system checks for molecular isotope beam formation, Patch panel installation, MELISSA laser window exchange, Liquid waste neutralization and solidification, MEDICIS mass separation, Front End inspection and repairs, RadioProtection detector check, Calibration and installation of a 2nd Kromek detector for collection monitoring and a Collimator system in development.

The conditioning of new electrode was successful. Dipole magnet calibration was checked. Gafchromic film was used to check the PSB proton beam position on the target. Safety tests from the departmental safety office/DSO are scheduled to take place before Easter holidays.

Restart is planned with stable beams. New target units will be constructed for radioisotopes of Tb, Tm, Ra, Ac and Cu, with a notable first uranium carbide UCx unit.

The GPS ISIS irradiation station is not available anymore, which means less irradiation opportunities will be available in 2024 as compared to 2023.

The ISOLDE and MEDICIS schedule have been released until end of August, with the inclusion of the MEDICIS schedule in the published ISOLDE schedule. The facility is planned to operate until protons stop in the middle of November.

With the introduction of KPI's, MEDICIS also now differentiates between production and development runs, as well as those collections foreseen for PRISMAP or MEDICIS.

A notable highlight is the collection of Ra/Ac-225, with a record efficiency of 54%, which for the first time allows a mass separation facility to collect more than what is lost in the separator and target as non-ionized isotopes. Two runs on Tb-155 were cancelled due to target unit failures after irradiation. Ba-128 collection was descoped for this year by CHUV as D. Viertl is occupied with PRISMAP projects. Sm-153 will be delivered on monthly bases, with provision of starting at the end of summer.

MEDICIS training activities are progressing with a PhD student, Edgars Mamis, finishing his PhD towards next summer, while a new PhD student, Patricija Kalninas, will be starting at the end of July. Cu-67 production capabilities will further be investigated across the year.

Valentina Garibotto inquires which radionuclide is foreseen to be used in a clinical settings, to which it is mentioned Sm-153 and Pb-212, both for Germany, while Pakistan is waiting to submit a project towards the use of Ac-225.

This morning at a tripartite meeting with both French and Swiss authorities, the MEDICIS licensing file was declared as appropriate for shipping radionuclides for clinical translation. If a Swiss hospital is to be involved, extra discussion will be triggered with OFSP.
Simone Gilardoni comments that this statement cannot be confirmed until official minutes and management approval is obtained at CERN. This originates from the tripartite rules which are strict and needs the advices of all the three members part of the tripartite agreement(Swiss, French, CERN).

Thomas Cocolios asked if MEDICIS has applied the Kromek GR-05 detector, for which Charlotte Duchemin answers that is had been positioned in the MEDICIS beamline, at the collection chamber position, next to the GR-1 detector, for high activities. He also inquired on the missing ISIS irradiation table on GPS station. Simone Gilardoni answers that this will need to be addressed during LS3, as the case is under investigation. Thierry Stora added this had been removed from GPS before the situation would degrade to a point where the GPS Front End could not be operational anymore. Some time is required to fully investigate the problem.

MEDICIS operation and infrastructure for preparation of clinical production

Laura Lambert presents an operational case with a typical timeline for collection of Sm-153 (see https://indico.cern.ch/event/1418414/contributions/5985359/attachments/2888605/5063349/LAMBERT_12th%20MEDICIS%20collaboration%20board%202024.pdf)

Ruslan Cusnir asks what impurities have been identified in Sm-153. Charlotte Duchemin replied that there are some traces of Eu-152 and Eu-154 on the imported (carrier added) source itself when it is shipped, while none of those can be detected on the collection foils on the high molar activity Sm-153 samples.

MED-034

The presence of low levels of Polonium radionuclides have been detected in some Ra/Ac-225 samples. It probably originates from PoO volatile and ionized molecules, possibly leaking from the neighbouring masses. Frank Bruchertseifer is surprised that the DGA resin/column could not separate this fraction out, as this had never been a problem at JRC.

Status report MED-037 / 032 (Alphamet/PRISMAP Ac225) NPL

Report was provided by Sean Collins. Thomas Cocolios suggests to hold a dedicated separated meeting between CHUV, NPL and KULeuven on Ac225 sample assessments from the different projects. Michael Lassman asked on how much activity was required to perform the imaging, to which Sean Collins answered 40 MBq.

Status report MED-024 / 030 (Ac-225 in Belgium) Jake Johnson

Presentation : https://indico.cern.ch/event/1418414/contributions/5985367/attachments/2888392/5062801/Medicis_board_Ac-sample-purity-JJ_v1.pdf

Ruslan Cusnir asked about the presence of Po209, as Po209 is normally used as a tracer to calibrate GC-MS to measure other Po radionuclides.
Thierry Stora comments that there were very different conditions of collection.

Thomas Cocolios comments that this will be updated with the different experiments and this is a preliminary report of the work, and it will be relevant to receive low temperature collection to see the differences.
Thierry finally asks about needs or prospects for IRA or NPL, to which IRA answers this is concluded while more needs to be done at NPL.
Thomas Cocolios informs the board that there is a campaign at the Isolde facility to do a in depth decay spectroscopy of Ac-225 and its progeny.

Report from PAEC by Inzamam Miam

Radiolabelling of Ac-225 at PAEC with DODATATE could be achieved. The radiochemical purity received was >90%, with an initial activity of 30 MBq. The labelling yield was very good. Through HPLC a yield of about 80% for the radiolabelling efficiency was obtained.

New projects

MED-038 Pre-clinical proof-of-concept of a novel CCR5-targeted radioligand cancer therapy strategy – presented by F. Bois.

Fred. Bois presents this preclinical project proposal, linked to the development of radiobioconjugates for CCR5.
It was mentioned that MEDICIS will stop operating with CERN protons drivers (PSB) in November 2025.
HUG will request 800 kBq per delivery. As pointed out by M. Lassmann, prior detector calibration is required before injecting in animals. Thierry Stora mentions this could be anticipated. Frank Bruchertseifer asks about the chelator used, which is DOTA, as already successfully tested for Lu/Ga.
The project is approved by the board, with the provision that 225Ac can only be delivered in 2025, or after 2 years long shutdown.

MED015 and LOI MED-039 – E. Mamis

This is a combined status report of MED-015 and a new proposal, Letter of Intent under MED-039.
Update on project MED-015 on Sc radionuclides developments:
Report was provided on the combination of target and ion source techniques to produce preclinical and clinical doses of Sc-44 and Sc-47. Collection efficiencies could reach about 2% and rates compatible with preclinical investigations. 2 scientific publications were produced, a bachelor and a master thesis produced. The project is expected to come to a conclusion, with an additional collection, and with the defense of the PhD of E. Mamis.
A new project is submitted. It concerns the separation of Terbium radionuclides, Tb-149/152/155, from prospective tantalum targets. It will also include the development of new nanostructures targets such as VC, VB and TiC. The main purpose is to complete some other ongoing projects.
Thomas Cocolios mentions that nanomaterials could be of interest. For which the nanolab would be required. At present TiC and VC are selected as prospective targets and would present less hazard. nanoCaO is for instance also available for ISOLDE.
Nick van der Meulen mentions that this is an interesting proposal and inquires if there is plans for an irradiation facility in Latvia. Edgars Mamis mentions that one private company operates a cyclotron center. It is as yet difficult to predict if the company is keen in developing research activities. Upon further inquiries on development work for Tb-149, Edgars answers that it will be done for Tb-155 in priority, and will notably consider release studies.

Collaboration work CERN/PK on radiochemistry developments – I. Miam

Inzamam Miam presented the latest activities on radiochemical developments, mainly on the development of a generator for Ra-224/Pb-212, and for the separation of radiolanthanides, such as Tb/Ln or Eu/Sm. Thierry Stora mentions that Ra/Pb-212 generator was used within PRISMAP for check of radiolabeling yield in DTU in 2023. Thomas Cocolios asks confirmation if we can deliver Pb212 from Ra224 collections, which is indeed the case. This could be made available to project proposals, notably from Belgium groups.

Closing remarks & proposal for anniversary of MEDICIS

In September, CERN management was issuing positive recommendation for the continuation of MEDICIS, following the very positive outcome of the international review . The conditions under which the facility could operate could follow up two baselines.
A second board towards the end of the year and maybe combined with the anniversary of MEDICIS will be proposed, for instance on 11 December to celebrate the anniversary of the first collection (11^{th} of December 2017).
Next board meeting will be in presence and combined with a little celebration, already looking into appropriate space around the Science Gateway or other symbolic places at CERN.