Chapter XI

SPES APPLICATIONS

11.1 Introduction

The SPES strategy is to develop a facility for Nuclear Physics research together with a facility for applied Physics based on the same technology and infrastructure. The dual-exit SPES cyclotron allows the operation of two targets at the same time, sharing the total current of 0.750 mA. To fulfill the ISOL production goal of 10^{13} fission/s in the target, a proton beam current of 200μA (40MeV) is needed; the second beam, up to 500μA 70MeV, will be devoted to applications; mainly neutron production for material research (NEPIR facility) and production of new isotopes for medical applications (LARAMED facility).

It should be considered that the activation of materials at a beam power of 20-30 kW, do not allow to operate the same target for long time. Considering a shift of two weeks with 2 days for beam preparation and 12 days of beam on target, considering 7 shifts for maintenance in one year, we can offer at least 5000 hours per year of beam dedicated to the ISOL targets and 5000 for applications.

A detail of the SPES layout is shown in Fig. 11.1; the proton beam can be sent to two ISOL target caves, two irradiation areas (mainly dedicated to neutron production) and to the radioisotopes production area.

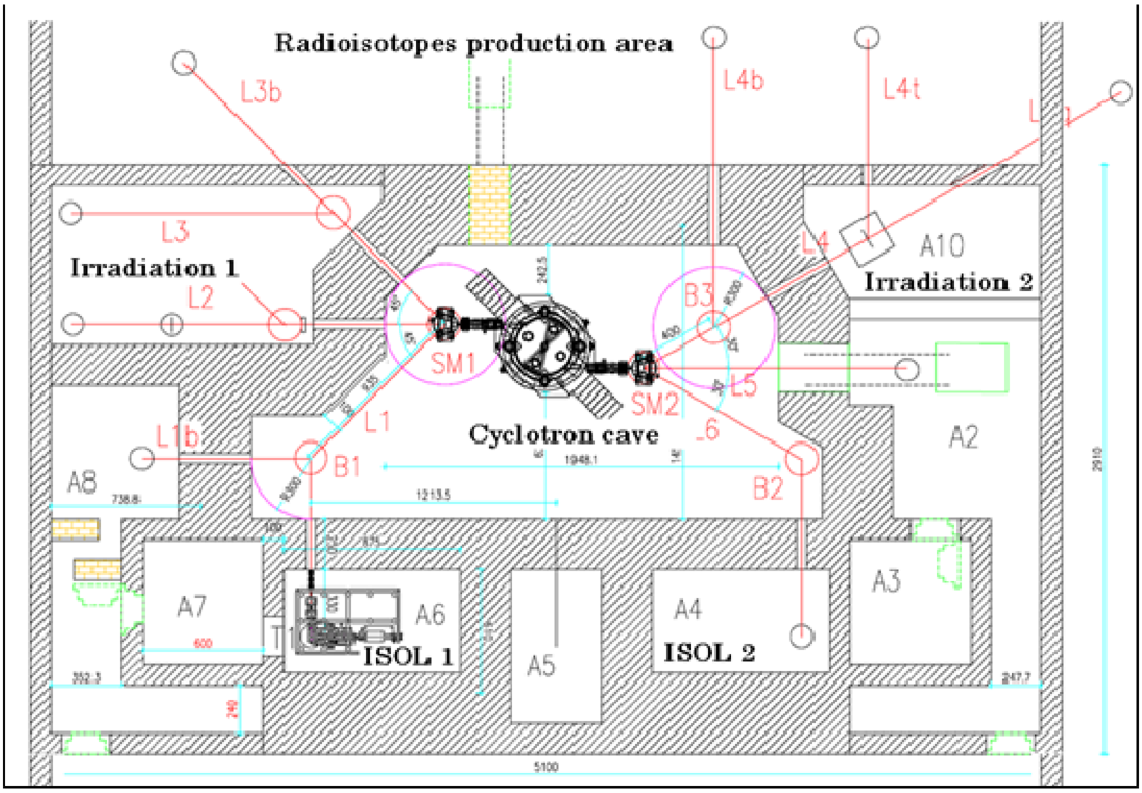


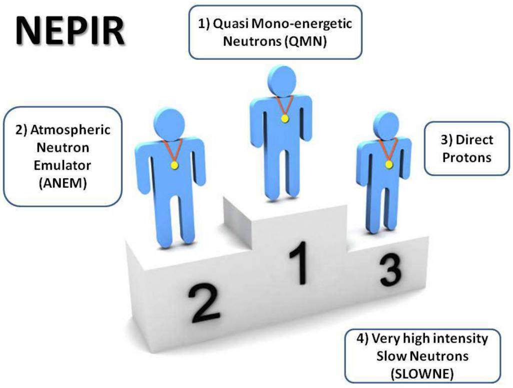
***Figure 11.1**: Partial layout of SPES. Proton beam distribution.*

11.2 The NEPIR neutron facility

The goal of the NEPIR project is to construct a versatile high flux fast neutron irradiation facility that would be unique in Italy and a reference point for European research, both applied, industrial and basic science.

NEPIR will use the protons of the SPES variable energy high current cyclotron to produce:

(1) an intense quasi mono-energetic neutron (QMN) beam with a controllable energy peak in the 35-70 MeV energy range;
(2) an intense beam of fast neutrons (E > 1 MeV) with a continuous energy distribution similar to that of atmospheric neutrons found at flight-altitudes and at sea-level (Atmospheric-Neutron EMulator, ANEM);
(3) a variable energy, low intensity beam of direct protons.



In addition, with lower priority, a high intensity slow neutron beam line (SLOWNE) is also foreseen. Application of this beam line is the study of neutron-material interaction of interest for transmutation studies of IVth generation Fast Reactors, an INFN-ENERGY research project. Other interests to the use of slowed neutrons come from neutron science applications, such as neutron imaging or prompt gamma activation analysis of materials and industrial/cultural artifacts. These applications would be developed in collaboration with the CNR.

The schematic layout of NEPIR is shown in fig.11.2. The vertical distribution of the QMN/ANEM beam line is shown in fig. 11.3. This solution optimizes the neutron background.

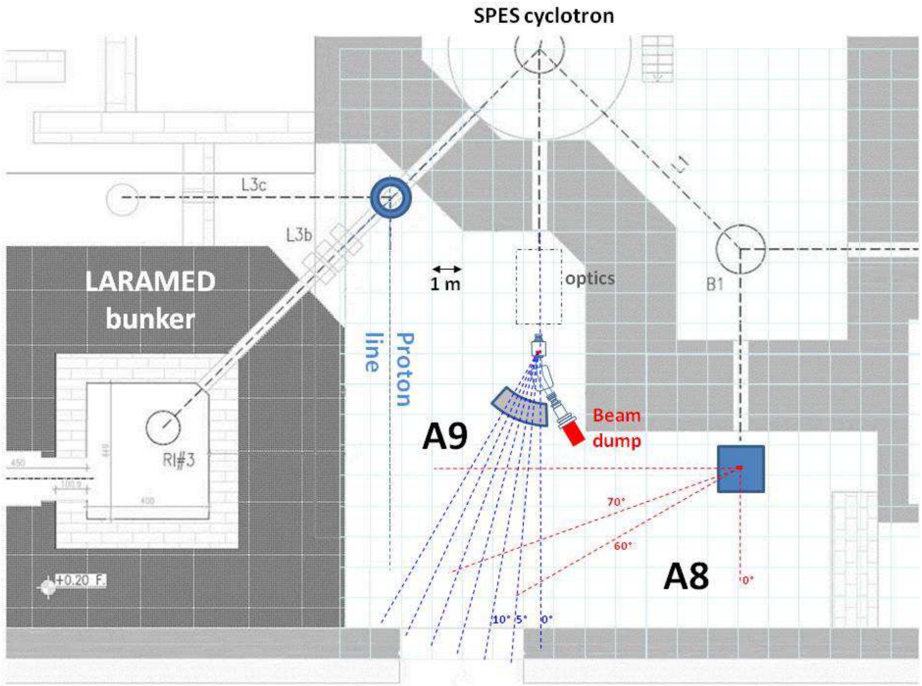


Figure 11.2: *Schematic floor plan of NEPIR, the neutron and proton irradiation facility at SPES (overlaid 1 m2 grid). The supplementary (local) shielding is not shown. The QMN and ANEM beam lines in hall A9 coincide and share the spent proton bending magnet, beam dump system (red rectangle) and multi-angle collimator system (shown indicatively; angles 5°-30°). The direct proton line is also in hall A9. The SLOWNE target system is in hall A8 (serviced by the B1 bending magnet). The LARAMED bunker on the lower left is dedicated to the production of radio-isotopes for medical applications.*

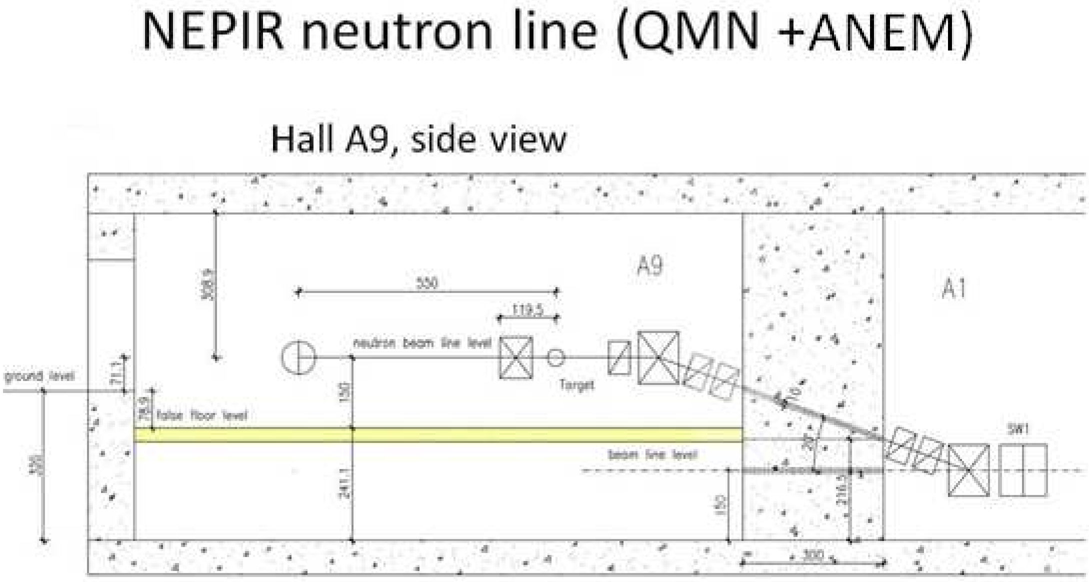


Figure 11.3*: Optics of halls A1 and A9 of the NEPIR neutron lines (QMN and ANEM). At the test point, the neutron beam is 1.50 m from the false floor (3.91 m from the bottom cement floor). The optics consists of two dipole magnets, two quadrupole doublets and a single one, and a bending magnet for the spent proton beam. The supplementary shielding is not shown.*

The primary purpose of NEPIR is to study radiation damage effects induced by atmospheric neutrons and solar protons in electronic devices and systems.

The QMN will be produced by an assortment of thin lithium and beryllium targets (1-4 mm thick). The proton energy and thickness of the thin targets are changed to produce nearly mono-energetic neutrons at several discrete energies. The protons that pass through the thin targets without causing nuclear reactions are deflected by a bending magnet and guided to a heavily shielded beam dump. A multi-angle collimator will be used to correct data taken in the forward (0°) direction, by subtracting data obtained at larger angles (typically in the 15°-30° range).

The neutron beam with atmospheric energy distribution will be produced with an innovative technique without the use of moderators by the ANEM system. It is based on a rotating composite target made of beryllium and a heavy element such lead or tantalum. It will produce atmospheric-like neutrons in the 1-70 MeV energy range: the incident proton beam impinges alternatively on the two materials and the neutron energy spectrum is directly shaped to resemble the seal-level atmospheric one without the use of moderators. The proton beam is not stopped by the target (to avoid damage of the Be): the spent low energy protons that emerge are magnetically deflected towards a beam dump; a simpler option under investigation is to stop them in a thin copper plate. R&D was performed in the framework of the 5th Scientific Commission of INFN (experiments LENOS and NEUTARG). The simulated neutron spectrum is shown in fig. 11.4 compared to the terrestrial spectrum of reference. The expected acceleration factor is $F=6*10^9$ with 50 μA proton beam on ANEM target, corresponding to a neutron flux of $\Phi_n(E>1MeV) \sim 3\times10^7$ n $cm^{-2}\cdot s^{-1}$. This means that one hour of irradiation is equivalent to six hundred thousand years of exposure at sea level.

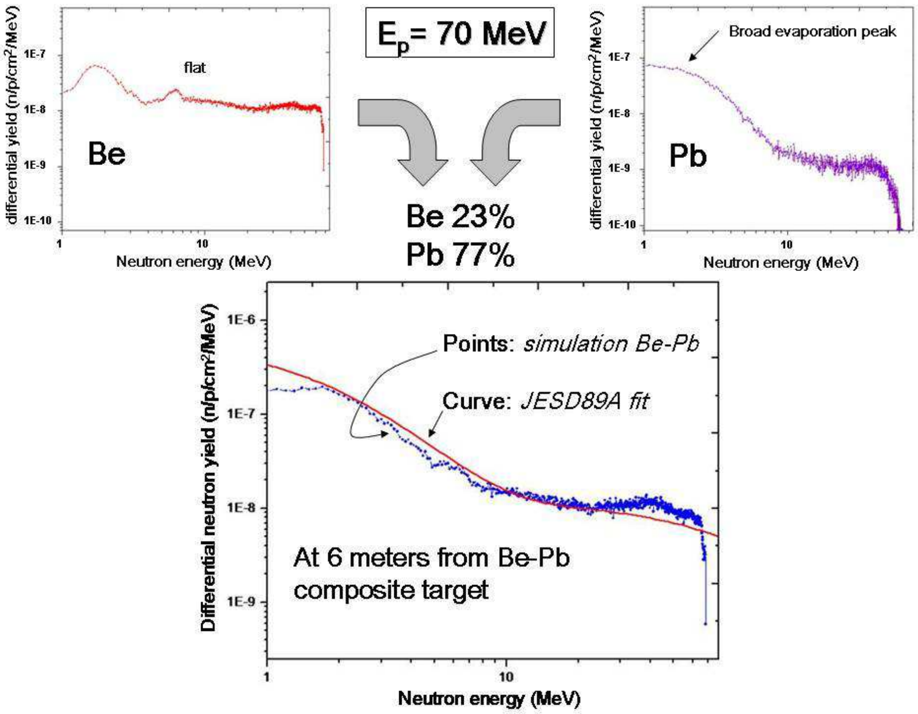


Figure 11.4: *The simulated differential neutron yields from 70 MeV protons on 26 mm Be (upper left) and 7 mm Pb (upper right), combined to form an effective atmospheric-like spectrum from 70 MeV protons (bottom). The JEDEC (JESD89A) standard reference curve is rescaled and shown for comparison.*

A comparison with others facilities is shown in fig.11.5 in lethargy representation.

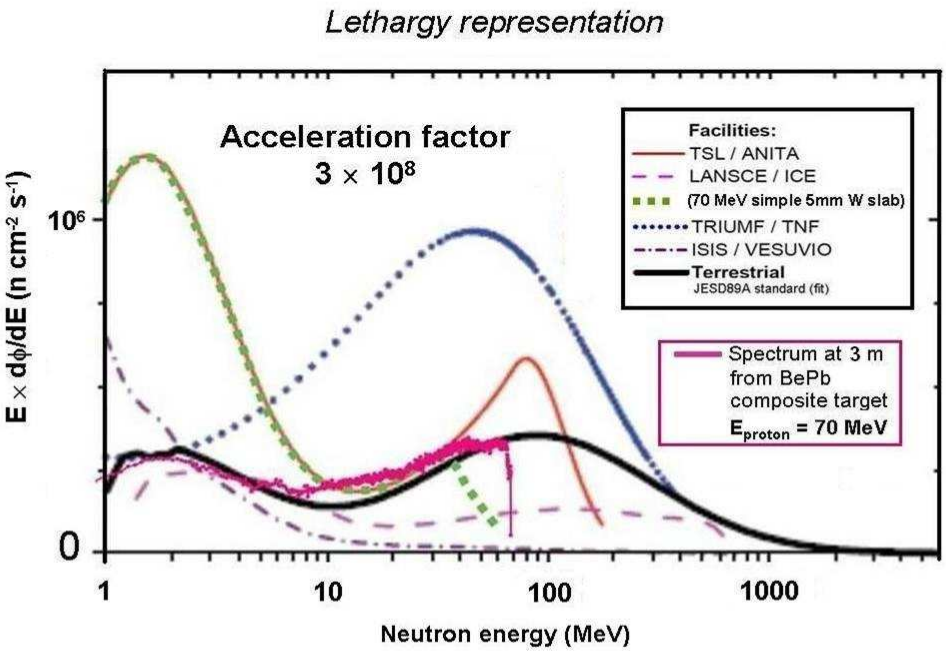


Figure 11.5: The lethargy differential neutron flux of 4 existing white-spectrum facilities. The black curve is the JEDEC (JESD89A) reference curve multiplied by 3×10^8. The simulated neutron spectrum (cyan) from 70 MeV protons on a Be-Pb (23%, 77%) rotating target at 6 m with I_{proton} ~ 5 μA resembles the atmospheric one in the 1-60 MeV energy range.

The estimated cost of the first phase of NEPIR (QMN and ANEM) is reported in Table 1. It is based on the optics reported in Figure 2. Although the table is for the moment not complete, we estimate the total cost at about 2 MEuros. At present NEPIR is in the design phase and is not funded.

Item (description)	Cost (kEuros)
Two dipoles (magnet + supply)	500
5 quadrupoles (magnet + supply)	500
Bending magnet of spent protons	125
Two faraday cups (hardware + control)	10
Two pumping groups	20
Platform structure in Al (65 m^2)	150
Beam dump	50
Multi-angle collimator structure	?
Supplementary shielding	?
QMN target system	50
ANEM rotating target system	150
total	About 2000

11.3 LARAMED laboratory for radionuclides in medicine

Radionuclides are fundamental components of nuclear medicine (NM) technology, which in turn constitutes one of the most important imaging modality and therapeutic approach for the treatment of many critical diseases. Correct functioning of NM is crucially dependent on the availability of essential radionuclides in sufficient amount to ensure widespread distribution to hospitals. Similarly, progress in NM is always tightly linked to the continuous development of effective production processes of novel radionuclides having peculiar nuclear properties that might help finding unprecedented solutions to unsolved clinical issues. The LARAMED project aims at exploiting the improved technical characteristics of the new, high-current, 70-MeV cyclotron, under installation at LNL, both to develop more efficient methods for the production of well-established radionuclides already playing a key role in NM, and to investigate yet unexplored production routes for novel radionuclides having potentially interesting nuclear properties for medical applications, but still not available in NM. Ultimately, the major objective of this project is to establish a establish a Science and Technology Centre with the aim to study, develop and produce innovative relevant medical radionuclides to be distributed to hospitals and clinical departments for both routine use in patients' treatment and clinical research purposes, leading to new healthcare improvements.

The main focus of LARAMED is on the study and development of efficient methods for the production of medical radionuclides using the new, high-beam-current, high-energy SPES cyclotron. The main research lines are the following:

1) development of a target technology suitable for operating with high-current, high-energy proton beams,

2) development of alternative, more efficient procedures for obtaining important medical radionuclides, including Tc-99m, Cu-64, Cu-67, I-124, Sr-82, Ge-68 and Zr-89 using a 70-MeV, 750-μA cyclotron,

3) high-precision determination and re-evaluation of cross-sections of relevant nuclear reactions employed for the production of medical radionuclides,

4) development of fully automatized radiochemical procedures for target processing, separation and purification of medical radionuclides, and

5) Design and development of novel radiopharmaceuticals for targeted guided imaging and therapy in oncology.

The project has a strong interdisciplinary trait, as it requires the key contribution of specialists coming from different disciplines including nuclear physics, radiochemistry and nuclear medicine. It offers a clear-cut example of application of fundamental knowledge in nuclear physics to stimulate progress in medicine for the final benefit of patients. Modern advances in diagnosis and therapy of important diseases have been made possible only through the fundamental contribution of physical sciences to medicine, and this project is expected to provide another significant example of this synergy eventually affording new technological advancements and clinical solutions.

A clear illustration of the remarkable degree of involvement of different public and private subjects is given by the participation to the project of research groups from INFN, CNR, various Universities and hospital centers, and of a private company that is interested in pursuing further the main scope of the project by establishing a pharmaceutical-grade production facility of the cyclotron-produced radionuclides and receiving marketing authorization for the commercial supply of the final radionuclide products.

These deeps intertwine between public and private sectors are expected to attract a sufficient amount of investment for completing the research program within the scheduled time. In turn, the successful accomplishments of the project will allow initiating the commercial distribution of final solutions of radionuclides having the required pharmaceutical quality for clinical use, a result that can ensure the economical self-sustainment of the whole process. This also emphasizes the high socio-economic value of this project generated by its impact on the local economy and on the healthcare system in general.

The Facility will be built on two levels:

- level -1 in which the irradiation stations will be installed (see Fig. 11.6). The beam extracted from the cyclotron will be transferred to the irradiation bunker. Three highly shielded bunkers at underground level allow the irradiation at high current of the production targets.

- level 0 in which the radiochemical laboratories will be realized (NOT GMP and GMP). The irradiated solid targets will be transferred to laboratories at level 0 where they are manipulated for the production of radionuclides (see Fig. 11.7).

The design shown in Figure 11.7 was created with the aim to optimize the use of quality control service (area indicated by the letter C) placing it at the center of two Radio pharmacies one of which is designed to work in production under GMP (areas indicated with the letter B) while the other will be used for the development of new molecules (the areas indicated with the letter D). This design allows rationalizing the spaces so as to ensure, where possible, that the maintenance operations are carried out in not classified areas thus preventing the break of the classes in the local production. The production of a medicine labeled with radioactive is subjected to two standards: GMP standards require that the production zone should be at positive pressure with respect to adjacent rooms in such a way as to prevent any external contamination from local more "dirty"; radioprotection rules require that local containing radioactive material are in negative pressure with respect to adjacent rooms, to prevent leakage of substances hazardous to health. In the proposed project, the two standards are applied in a harmonious way creating at the level of radiochemical laboratories (level 0) a hole in the local "Filter" B5 (-40 Pa). The local "White Room" B2 (0 Pa) and "Local Vestibule" B3 (-10Pa) and B4 (-25 Pa) are in a chain of positive pressure from production local to the outside (in accordance with the prescribed GMP standards), while the hole pressure ensures that any radiation leaks are confined to the local B5 (according to radiation protection).

The total cost of the project , estimated in 41.9 M€, includes 40.85 M€ of materials , equipment , infrastructures, management support costs and overhead (only applied to costs covered by co-financing Best Medical International and INFN) plus 1.05 M€ of personnel cost.

An external funding is expected by collaboration with private medical companies for an investment around 13.5 M€ (32% of the total cost of the project) in equipment for the LARAMED Facility: equipment for radionuclide and pharmaceutical laboratories, for cyclotrons, beam lines, targets and for the commercial supply of the final radionuclide.

INFN has already invested 20.0 M€ in the SPES project that includes a 70-MeV cyclotron able to deliver 750-μA of beam current and the related infrastructures. This is an in-kind contribution.

The project has been financed with 7.8 M€ by the Ministry (by the call “Premium Projects 2012”) as detailed in the following Project Costs Estimation Table.

- 0.45 M€ are dedicated to CNR Research Activities

- 7.35 M€ are dedicated to INFN Research Activities

INFN, CNR and Universities will cover the cost of their own personnel involved in the project activities, as an in-kind contribution.

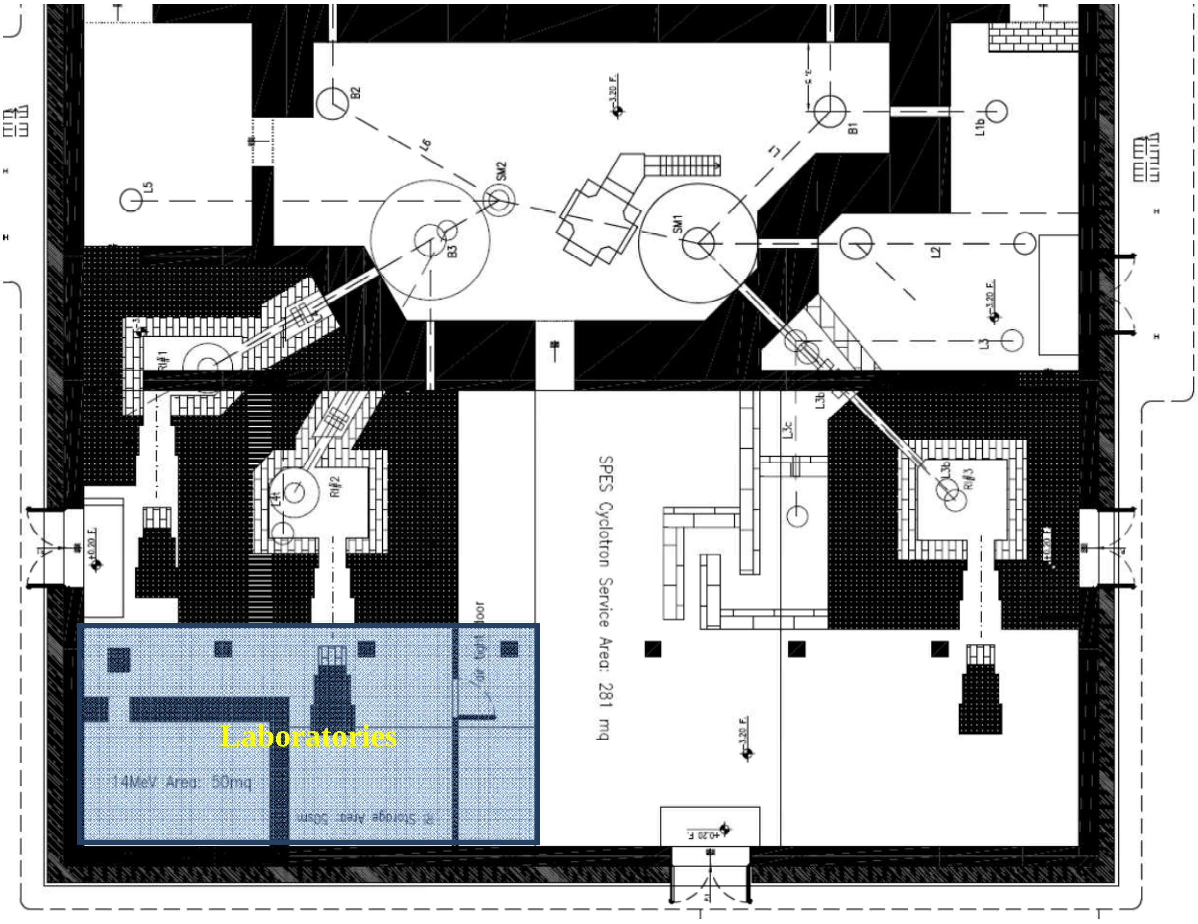
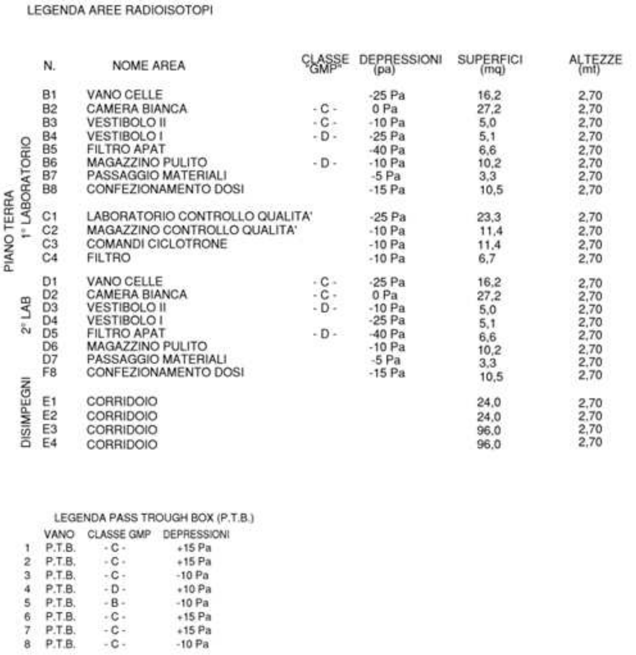


Figure 11.6: layout of LARAMED irradiation areas.


LEGENDA AREE RADIOISOTOPI

	N.	NOME AREA	CLASSE "GMP"	DEPRESSIONI (pa)	SUPERFICI (mq)	ALTEZZE (mt)
PIANO TERRA 1° LABORATORIO	B1	VANO CELLE		-25 Pa	16,2	2,70
	B2	CAMERA BIANCA	- C -	0 Pa	27,2	2,70
	B3	VESTIBOLO II	- C -	-10 Pa	5,0	2,70
	B4	VESTIBOLO I	- D -	-25 Pa	5,1	2,70
	B5	FILTRO APAT		-40 Pa	6,6	2,70
	B6	MAGAZZINO PULITO	- D -	-10 Pa	10,2	2,70
	B7	PASSAGGIO MATERIALI		-5 Pa	3,3	2,70
	B8	CONFEZIONAMENTO DOSI		-15 Pa	10,5	2,70
	C1	LABORATORIO CONTROLLO QUALITA'		-25 Pa	23,3	2,70
	C2	MAGAZZINO CONTROLLO QUALITA'		-10 Pa	11,4	2,70
	C3	COMANDI CICLOTRONE		-10 Pa	11,4	2,70
	C4	FILTRO		-10 Pa	6,7	2,70
2° LAB	D1	VANO CELLE	- C -	-25 Pa	16,2	2,70
	D2	CAMERA BIANCA	- C -	0 Pa	27,2	2,70
	D3	VESTIBOLO II	- D -	-10 Pa	5,0	2,70
	D4	VESTIBOLO I		-25 Pa	5,1	2,70
	D5	FILTRO APAT	- D -	-40 Pa	6,6	2,70
	D6	MAGAZZINO PULITO		-10 Pa	10,2	2,70
	D7	PASSAGGIO MATERIALI		-5 Pa	3,3	2,70
	F8	CONFEZIONAMENTO DOSI		-15 Pa	10,5	2,70
DISIMPEGNI	E1	CORRIDOIO			24,0	2,70
	E2	CORRIDOIO			24,0	2,70
	E3	CORRIDOIO			96,0	2,70
	E4	CORRIDOIO			96,0	2,70

LEGENDA PASS TROUGH BOX (P.T.B.)

	VANO	CLASSE GMP	DEPRESSIONI
1	P.T.B.	- C -	+15 Pa
2	P.T.B.	- C -	+15 Pa
3	P.T.B.	- C -	-10 Pa
4	P.T.B.	- D -	+10 Pa
5	P.T.B.	- B -	-10 Pa
6	P.T.B.	- C -	+15 Pa
7	P.T.B.	- C -	+15 Pa
8	P.T.B.	- C -	-10 Pa

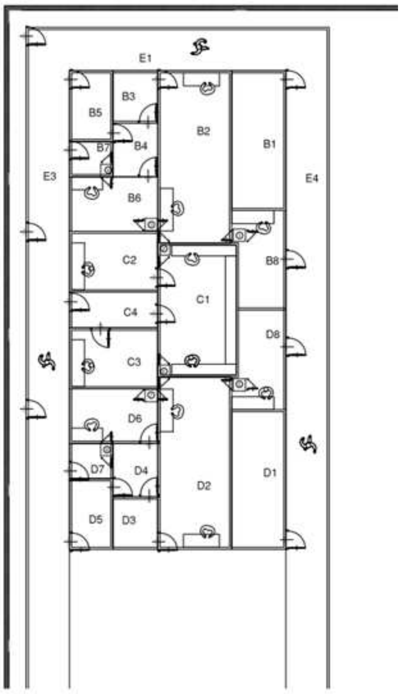
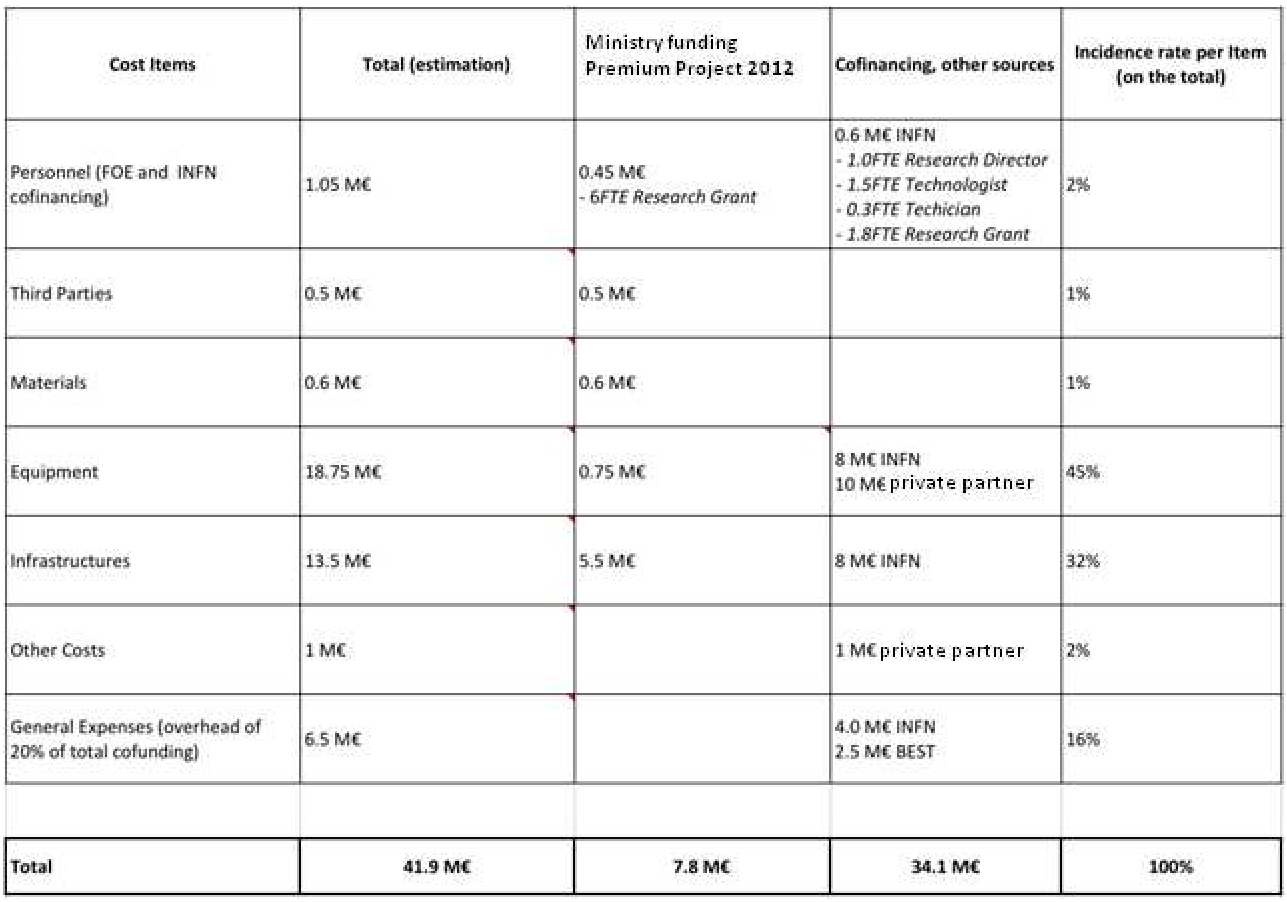


Figure 11.7*: Layout of radiochemical laboratories at level 0 and description of the areas.*

LARAMED Project Costs Table



Cost Items	Total (estimation)	Ministry funding Premium Project 2012	Cofinancing, other sources	Incidence rate per Item (on the total)
Personnel (FOE and INFN cofinancing)	1.05 M€	0.45 M€ - *6FTE Research Grant*	0.6 M€ INFN - *1.0FTE Research Director* - *1.5FTE Technologist* - *0.3FTE Techician* - *1.8FTE Research Grant*	2%
Third Parties	0.5 M€	0.5 M€		1%
Materials	0.6 M€	0.6 M€		1%
Equipment	18.75 M€	0.75 M€	8 M€ INFN 10 M€ private partner	45%
Infrastructures	13.5 M€	5.5 M€	8 M€ INFN	32%
Other Costs	1 M€		1 M€ private partner	2%
General Expenses (overhead of 20% of total cofunding)	6.5 M€		4.0 M€ INFN 2.5 M€ BEST	16%
Total	**41.9 M€**	**7.8 M€**	**34.1 M€**	**100%**