



# A Cyclotron Production Center

*A Center of Excellence*

*A powerful tool to boost technological R & D and commercial activities  
with a strong social impact*

*Draft Proposal*

**2016**

*Energy Life Sàrl, Avenue des Morgins 27, Genève 1213, Switzerland  
Tel.: +41 79 1933545, [info@energylife-ge.com](mailto:info@energylife-ge.com)*

*[www.energylife-ge.com](http://www.energylife-ge.com)*



Object of the current revision: First document

Total number of pages (text and appendixes) = 29 pages + 0 pages of appendixes

EXTERNAL DIFFUSION:

INTERNAL DIFFUSION:

Energy Life for internal review

REVISION TABLE

A					
0	27/06/2016				
		J. Galvez			
REV	DATE	WRITER	CHECKER	QA CHECKER	APPROVER
NAMES & SIGNATURES					

REVISIONS

Rev.	Date	Chapter	Page	Object	Author
1	27/06/2016	all	all	First edition	J. Galvez
2			I		

## Table of Contents

<b><u>ABOUT US .....</u></b>	<b><u>5</u></b>
<b><u>EXECUTIVE SUMMARY.....</u></b>	<b><u>5</u></b>
<b><u>MISSION .....</u></b>	<b><u>7</u></b>
<b><u>SCIENTIFIC RESEARCH AND EDUCATION.....</u></b>	<b><u>8</u></b>
<b><u>RADIOISOTOPE PRODUCTION FACILITY.....</u></b>	<b><u>9</u></b>
<b><u>DESIGN COST .....</u></b>	<b><u>12</u></b>
<b><u>CYCLOTRON FABRICATION COSTS .....</u></b>	<b><u>12</u></b>
<b><u>MARKET OVERVIEW .....</u></b>	<b><u>14</u></b>
<b><u>DIAGNOSTIC RADIOPHARMACEUTICAL MARKET IN EUROPE .....</u></b>	<b><u>15</u></b>
<b><u>THERAPY RADIOPHARMACEUTICAL MARKET IN EUROPE.....</u></b>	<b><u>19</u></b>
<b><u>FINANCIAL PLAN.....</u></b>	<b><u>21</u></b>
<b><u>RECOMMENDATIONS.....</u></b>	<b><u>26</u></b>
<b><u>CONCLUSIONS.....</u></b>	<b><u>26</u></b>
<b><u>REFERENCES.....</u></b>	<b><u>27</u></b>

## About us

Energy Life SARL (ELife) is a Swiss company aiming to bring innovative products and services in the domain of radiopharmaceutical production using innovative methods and devices and also in other domains related to energy production.

The company is proposing cutting edge technologies and also services to implement specific business models, which allow to implement challenging projects by bringing together the institutions and the needed capital through a specialized business model and a detailed business.

The potential to bring innovative technologies together with business ideas and financial support is one of the main characteristics of the company composed of a group of highly competitive business professionals and scientists. It consists of people with long experience in their particular domains and young energetic specialists.

The company is operating in the fields of science aiming to bring real benefit to the society and will make peoples life better and longer.

## Executive Summary





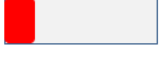


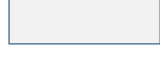
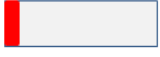
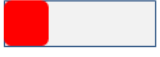

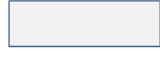
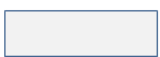
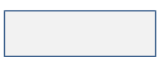


Positron-emission tomography (PET) and single-photon emission computed tomography (SPECT) are the most appropriate and common used methods for the diagnosis mainly of cancer and heart diseases and also, through scientific R&D programs, for brain disorders.

PET and SPECT molecular imaging involve the use of radiopharmaceuticals produced by means of specific accelerators and nuclear reactors.

The advancement of this field depends on the continuous development and validation of new, more sensitive and specific radiopharmaceuticals, based on the use of bio-conjugation and radiolabeling strategies, as well as by the diversification of the portfolio of radionuclides available for biomedical research.

These activities may take place only in specialized research centers, with the participation of highly qualified and specialized scientists involved in specific research and development. (*Institutions in the country*) are known to be the most advanced research centers involved in this type of activities.

Considering the importance to dispose of a specific infrastructure that can make available the continuously growing demand of medical radioisotopes, ELife is proposing the creation of Center of Excellence based on a cyclotron with dual beam of 30-70 MeV protons at up to hundreds of microamperes. The design and operational characteristics of the cyclotron create a versatile facility to support R&D, production of radioisotopes and nuclear physics research, as well proton therapy (eye tumor therapy) (Figure 1).

		Energy range			
Products		Up to 20 MeV	Up to 30 MeV	Up to 75 MeV	More than 75 MeV
Diagnosis	PET				
	SPECT				
Treatment	$\alpha/\beta$ Emitters others				
	Proton/ ion therapy				

*Figure 1: Cyclotron application in Nuclear medicine*

Medical accelerators may have many specific characteristics and we might group them in four main categories according to their energy range. Other parameters like beam intensity and type of accelerated particles (protons, deuterons, ions) are also very important depending on their use.

The key component for the proposed facility is a 70 MeV dual-extraction, multi-particle cyclotron. This cyclotron is similar to a fully operational commercial accelerator installed at the ARRONAX facility in Nantes, France.

The Center of Excellence will have the option to choose between a dual-extraction, multi-particle cyclotron in the energy range of 70 MeV or 30 MeV. ELife will adopt accordingly the business scenario in order to obtain a profitable center. The installation of such cyclotron at high energy is motivated by needs in matters of fundamental and clinical research in areas that require a strong scientific and technological cooperation between, nuclear oncology and radiochemistry, two disciplines well established at present.

The objective of this Center of Excellence is the design, production and use of radioisotopes for the benefit of research in nuclear medicine in the research centers and hospital services.

Nuclear medicine, little known by the public, is practiced by more than 40 years. Involves administration of radiopharmaceuticals for diagnosis (for scintigraphic imaging) or treatment (therapy).

The PET method mainly uses  $^{18}\text{F}$  radioisotope that has a short half-life, less than two hours. Therefore, should be produced near the point of use to prevent damage in transport. Thus, a low-energy cyclotron, designed only to produce  $^{18}\text{F}$  can be installed in a location near a hospital to meet its own needs.

## Mission

ELife's mission is to create and manage a state of the art facility, which will allow the Center of Excellence to work in collaboration with the world's leading specialists, to research and produce and distribute radioisotope products at the highest standards of quality, safety and service under the "Swiss Made" Brand. The major mission of the proposed state of the art high current, multi-particle 30-70 MeV cyclotron-based radioisotope production facility will be tasked to:

- Produce commercial radioisotopes,
- Produce research radioisotopes and other radioisotopes of emerging importance,
- Produce radioisotopes based on the concept developed at CERN for producing SPECT radioisotopes as  $^{99m}\text{Tc}$ ,
- Conduct R&D on all aspects of radioisotope production,
- Educate and train scientists, engineers, and technicians in related fields.

Commercial suppliers are responding by providing a range of cyclotrons of medium energy (30 MeV) proton accelerators. Table 1 lists radioisotopes typically produced with medium energy proton accelerators by commercial facilities.

In many cases, hospitals and universities produce PET radiopharmaceuticals for their own use while the commercial partner markets any excess PET radiopharmaceutical capacity to other near-by hospitals and clinics.

A 70 MeV cyclotron-based radioisotope facility will certainly complement the existing accelerator facilities for the cost effective production of a range medical and industrial radioisotopes. It will be able to supply the following radioisotopes:  $^7\text{Be}$  (53.3 d),  $^{22}\text{Na}$  (2.6 y),  $^{28}\text{Mg}$  (21h),  $^{47}\text{Sc}$  (3.4 d),  $^{52}\text{Fe}$  (8.3h),  $^{55}\text{Co}$  (17.5h),  $^{64}\text{Cu}$  (12.7h),  $^{65}\text{Zn}$  (244 d),  $^{66}\text{Ga}$  (9.4h),  $^{67}\text{Cu}$  (61.9h),  $^{68}\text{Ge}$  (271d),  $^{73}\text{As}$  (80.3 d),  $^{81}\text{Rb}$  (4.58h),  $^{82}\text{Sr}$  (25.34d),  $^{86}\text{Y}$  (14.7 h),  $^{89}\text{Zr}$  (78.4h),  $^{97}\text{Ru}$  (2.89d),  $^{122}\text{Xe}$  (20.1h),  $^{124}\text{I}$  (4.15 d),  $^{128}\text{Ba}$  (2.43d),  $^{117m}\text{Sn}$  (13.6d).  $^{68}\text{Ge}$ , with a half-life of 271d, is the main positron source used for calibration of PET cameras, and the  $^{82}\text{Sr}$  is the parent of  $^{82}\text{Rb}$  (1.27 m) used exclusively in myocardial imaging.

The capacity for the cyclotron facility is to provide approximately 2000 hours per year of 70 MeV proton beam time in dual beam mode, and an additional 3000 hours per year of dedicated beam of any available particle and energy. This will allow not only significant isotope production R&D, but also make available significant time to enhance domestic isotope production.

Table 1: Commercial radioisotopes produced in 30 MeV and low energy cyclotrons

Isotope	Half-life	Decay Mode	Nuclear reaction	Application
<b>Commercial radioisotopes produced in 30 MeV cyclotrons</b>				
$^{86}\text{Y}$	14.7h	$\beta^+$	$^{86}\text{Sr}(p, n)$	PET
$^{81}\text{Rb}$	4.6h	$\otimes$	$^{82}\text{Kr}(p, 2n)$	$^{81}\text{Rb}/^{81m}\text{Kr}$ generator
$^{67}\text{Ga}$	3.3 d	EC	$^{68}\text{Zn}(p, 2n), ^{66}\text{Zn}(d, n)$	SPECT
$^{201}\text{Tl}$	73.1h	$\otimes$	$^{203}\text{Tl}(p, 3n)^{201}\text{Pb} \rightarrow ^{201}\text{Tl}$	SPECT
$^{124}\text{I}$	4.2 d	EC(75%), $\beta^+$	$^{124}\text{Te}(p, n)$	PET label
$^{123}\text{I}$	13.2 h	EC	$^{122}\text{Te}(d, n), ^{123}\text{Te}(p, n),$ $^{124}\text{Xe}(p, 2n)^{123}\text{Cs}$ (decay)	SPECT
$^{111}\text{In}$	2.8 d	EC	$^{110}\text{Cd}(d, n)$ or $^{111}\text{Cd}(p, n),$ or $^{112}\text{Cd}(p, 2n)$	SPECT
$^{103}\text{Pd}$	17 d	EC	$^{103}\text{Rh}(p, n)$	Therapy
<b>PET radioisotopes produced in low energy cyclotrons</b>				
$^{11}\text{C}$	20.4 m	$\beta^+$	$^{11}\text{B}(p, n), ^{10}\text{B}(d, n)$	PET label
$^{15}\text{O}$	2.0 m	$\beta^+$	$^{14}\text{N}(d, n)$	PET label
$^{18}\text{F}$	1.82 h	$\beta^+$	$^{18}\text{O}(p, n)$	PET label
$^{64}\text{Cu}$	12.7h	$\beta^+$	$^{64}\text{Ni}(p, n)$	PET-Research

## Scientific Research and Education

The proposed Center of Excellence will be flexible enough to support radioisotope-based experiments and production and to support experiments in nuclear physics and chemistry.

This facility will allow scientists to make contributions in many fields of study, including:

- Providing a reliable supply of research radioisotopes to support the development and clinical trials of emerging radio-pharmaceuticals,
- Development of high-power radioisotope production targets,
- Production of radioactive ions for the study of the structure of nuclei far from stability,



- Measurement of excitation functions and reaction cross-sections that are relevant to radioisotope production and to the study of stellar explosions and nucleosynthesis in space,
- Measurement of thick target yields for radioisotope production,
- Fundamental research in nuclear chemistry, radiochemistry and experiments in material science.

The capability to accelerate alpha ( $\alpha$ ) particles and deuterons (D), provides for the R&D the production of the following radioisotopes:  $^{44}\text{mSc}/^{44}\text{Sc}$  (2.4 d/3.9 h),  $^{52}\text{Fe}$  (8.3 h),  $^{55}\text{Co}$  (17.5 h),  $^{67}\text{Cu}$  (61.9 h),  $^{68}\text{Ge}/^{68}\text{Ga}$  (271 d/68 m),  $^{86}\text{Y}$  (14.7 h),  $^{89}\text{Zr}$  (3.27 d),  $^{124}\text{I}$  (4.15 d),  $^{211}\text{At}$  (7.2 h),  $^{229}\text{Th}/^{225}\text{Ac}$  (7340 y/10 d). Radiopharmaceuticals based on  $^{211}\text{At}$  are currently being developed for targeted alpha therapy.

An aspect of the proposed facility will be the balance between production of R&D radioisotopes and routine production of industrial and medical radioisotopes. A cyclotron, capable of delivering proton (30-70 MeV, 350  $\mu\text{A}$ ) and alpha (70 MeV, 35  $\mu\text{A}$ ) beams will have three applications: nuclear medicine, radiochemistry and industry, the main application being research and the major objective the preparation of innovative radionuclides for biomedical and clinical research.

## Radioisotope Production Facility

The proposed cyclotron-based isotope production facility include:

- Dual-extraction, multi-particle cyclotron,
- Target stations and associated systems,
- Shielded radioisotope target vault,
- Beam transport lines,
- Shielded transfer station.

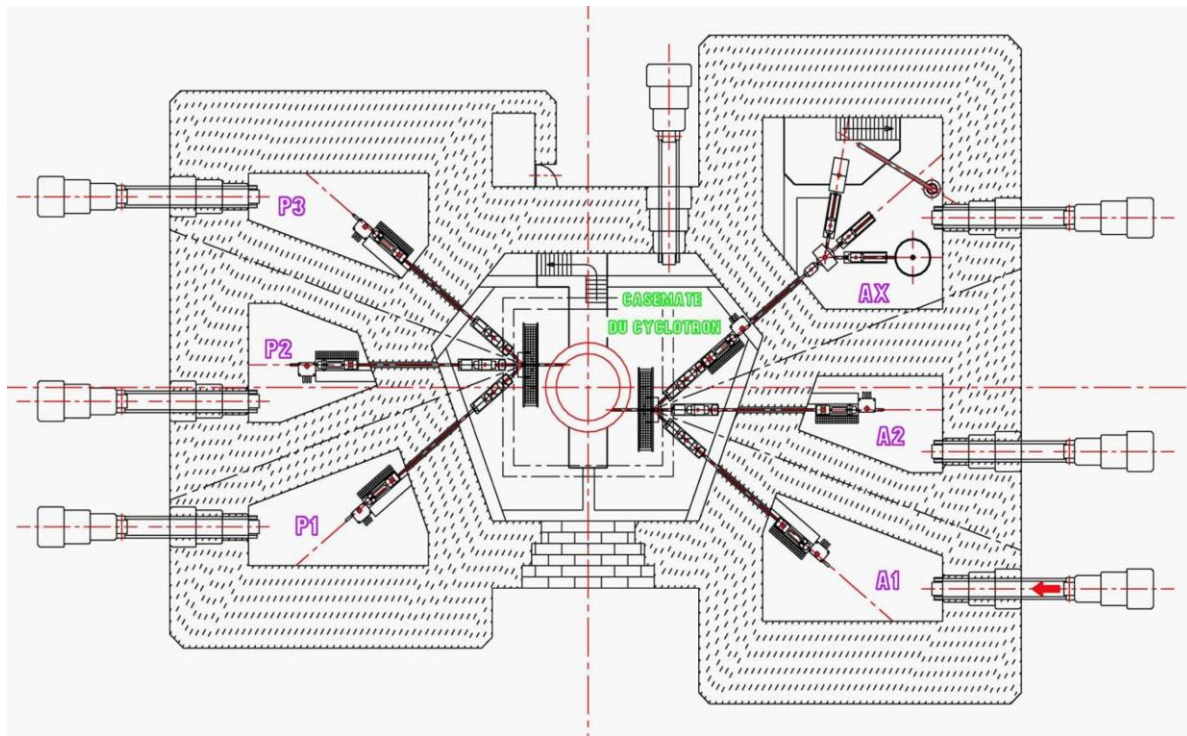
The accelerator is equipped with two external ion sources to produce 4 types of particles (Table 2), in particular high intensity, variable energy H<sup>-</sup> (30 – 70 MeV, 350 $\mu\text{A}$ ) and fixed energy  $^4\text{He}^{2+}$  (70MeV, 35 $\mu\text{A}$ ).

*Table 2: Parameter of the production facility (IBA Cyclone®70)*

Accelerated beam	Extracted Energy (MeV)	Beam Intensity ( $\mu\text{A}$ )
H <sup>-</sup>	30-70	350 (dual)
D <sup>-</sup>	15-35	50 (dual)
$^4\text{He}^{++}$	70	35 (single)
H <sub>2</sub> <sup>+</sup>	35	50 (single)

The cyclotron shall be capable of producing a large spectrum of radioisotopes (PET, SPECT and Therapeutic) and is composed of two exit ports allowing for dual beam extraction for protons and deuterons. Alphas and molecular hydrogen are exclusively extracted on the electrostatic extraction port.

The infrastructure required to install the cyclotron and its beam lines is illustrated in Figure 2. It illustrates the main cyclotron vault surrounded by six irradiation vaults. The building is 40 m long and 28 m wide and composed of 10000 m<sup>3</sup> of concrete.



*Figure 2: Cyclotron building, Arronax in France.*

Through two ports and using two external switching magnets, the cyclotron can deliver beam to six different beam lines. Each beam line has its endpoint in a separate vault. One of the three beam lines installed in the beam port equipped with the electrostatic deflector is divided into three lines (much shorter) within the corresponding vault.

Each line is composed of multiple magnetic elements for focusing and steering as well as diagnostic equipment (faraday cups, viewers, profilers, current measurement).

The master schedule of the project can be summarized as follows:

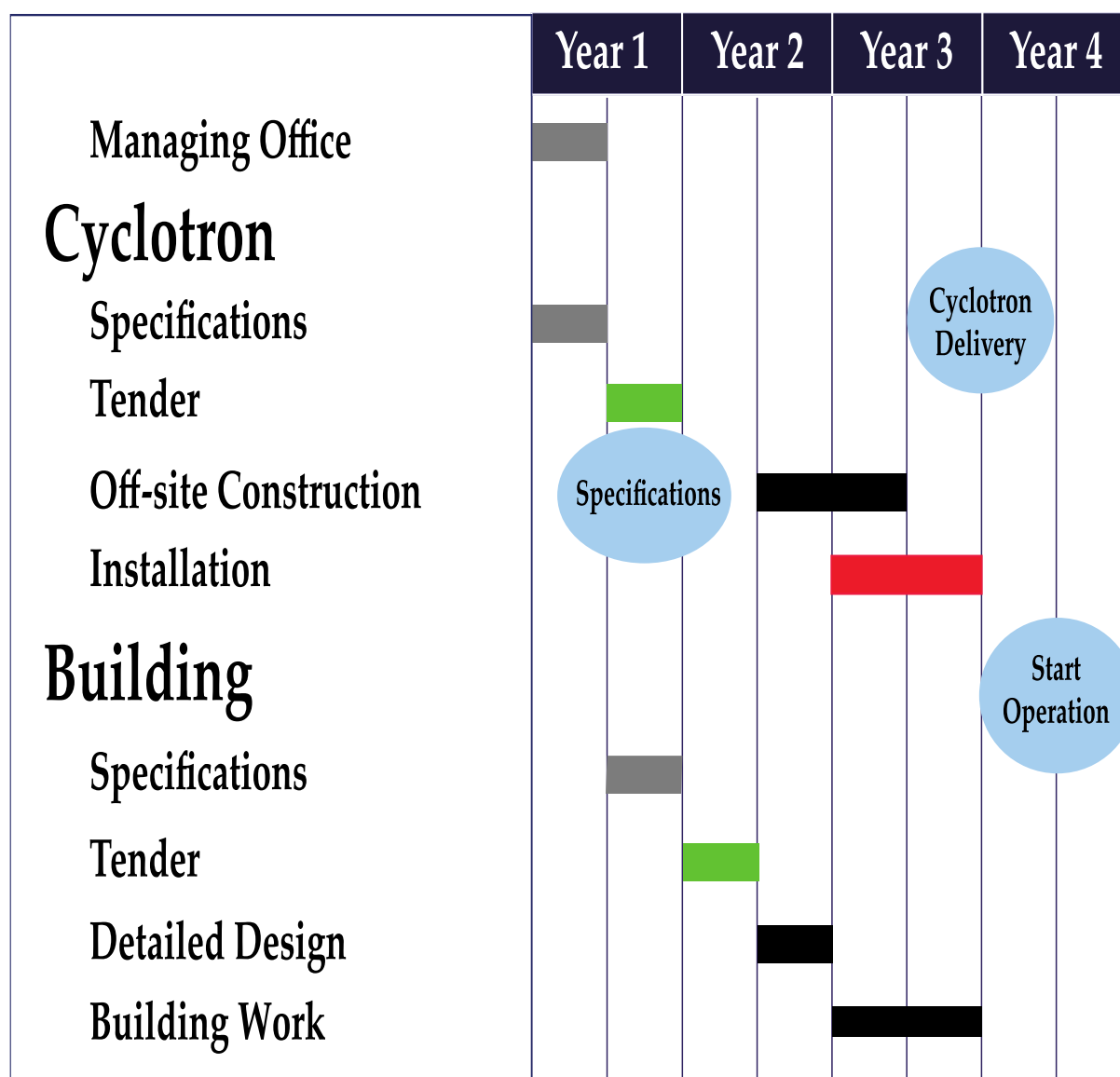


Figure 3: The master schedule

Two cyclotron credible vendors may have the ability to design and build either 30 MeV or 70 MeV cyclotrons. One of them won the bid for the cyclotron at the University of Nantes (70 MeV, 350  $\mu$ A beam current), which is similar to the operational specifications of this proposal.

These providers are:

- IBA Technology Group in Belgium and
- Advanced Cyclotron Systems, Inc. in British Columbia, Canada.

Both IBA and Advanced Cyclotron Systems and Technologies Group use very similar design in their 30 MeV cyclotron.

## Design Cost

An estimation of the design cost of the cyclotron of 30 MeV and 70 MeV is given in Table 3. It shows an average work rate of about 100 CHF/hour for design engineering labor for the 30 MeV and 70 MeV designs (1CHF is  $\approx$  1\$USD).

Table 3: Estimated design cost

Design Elements	Cyclotron Peak Energy			
	30 MeV		70 MeV	
	Labor Hours	Cost (KCHF)	Labor Hours	Cost (KCHF)
Physics Design	4000	400	4000	400
Magnet Detail	2000	200	2000	200
RF Design	2000	200	2000	200
Vacuum Detail	2000	200	2000	200
Beam line Detail	2000	200	2000	200
Subtotal	12000	1200	12000	1200
Contingency (50%)		600		600
Total Design Cost		1800		1800

## Cyclotron fabrication costs

The nominal budget cost of 1 mA, 30 MeV commercial cyclotron is 8 MCHF. If we apply a factor of 1.4 for a 70 MeV cyclotron, its cost will be about 11 MCHF.

For the calculation of the beam lines cost, we apply the same factor (1.4) to the total cost of 3 MCHF of a 30 MeV, then for a 70 MeV machine, its cost will be around 4 MCHF. See Table 4.

Table 4: Summary of Total Estimated Costs for the Cyclotron System

Cost Element	Cyclotron Peak Energy	
	30 MeV	70 MeV
Cyclotron Design Cost	0	1.8 MCHF
Cyclotron Fabrication Cost	8.0 MCHF	11.2 MCHF
Beamline Fabrication Cost	3.0 MCHF	4.0 MCHF
Total Acquisition Cost	11.0 MCHF	17.0 MCHF

From this table, we note the difference of 6 MCHF out of a total of approximately 17 MCHF between the estimated purchase price of a 30 MeV and a 70 MeV cyclotron.

In Table 5 is illustrated a comparison of two different facility centers, one operated with a 30 MeV cyclotron and the second with a 70 MeV Cyclotron.

Table 5: Comparison costs of 30 & 70 MeV Cyclotrons

DESCRIPTION	30 MeV	70 MeV
Management Office setup expenses	1.71	1.71
First three years	1.28	1.28
Building Design Phase		
Conventional Facilities Costs	1.00	1.20
Technical Facilities	0.75	0.90
Conventional Design PM Costs	0.25	0.40
<b>Sub-Total – Building Design Cost</b>	2.00	2.50
<b>BUILDING CONSTRUCTION PHASE</b>		<b>0</b>
Conventional Facilities	6.00	7.00
Construction Management	0.40	0.40
Insp., Des. & Project Liaison, Checkout & Accept.	0.10	0.10
Subtotal – Building Construction Cost	6.50	7.50
<b>Total Cost Design and Construction Phase</b>	<b>8.50</b>	<b>10.00</b>
<b>TECHNICAL FACILITIES</b>		
Cyclotron / Beamline / Vacuum / Support	8.60	12.00
Target System	0.40	0.40
Target Handling & Radioisotope Transport System	0.50	0.50
Instrumentation/Controls/Safety Interlocks	0.50	0.50
High Radiation Water System	1.00	1.00
<b>Subtotal – Technical Facilities</b>	<b>11.00</b>	<b>14.40</b>
<b>RADIOISOTOPE PRODUCTION</b>		
Quality Control (QC)	0.50	0.50
Radiation Monitoring	0.50	0.50
Radio-Chemical	1.50	1.50
Receiving station	0.30	0.30
Recovery	0.30	0.30
Deposition	0.10	0.10
Hot Cells (5 min)	3.00	3.00
<b>Subtotal – Radioisotope production</b>	<b>6.20</b>	<b>6.20</b>
<b>OTHER COSTS</b>		
Project Management	1.80	1.80
Health, Safety	<i>Included in Construction</i>	
Subtotal – Other Costs	1.80	1.80
<b>TOTAL – ACQUISITION COST</b>	<b>30.48</b>	<b>35.38</b>
<b>CONTINGENCIES</b>	<b>0.00</b>	<b>0.00</b>
Design Phase	0.20	0.25
Construction Phase	0.65	0.75
Technical Phase	1.10	1.44
<b>TOTAL – CONSTRUCTION CONTINGENCY</b>	<b>1.95</b>	<b>2.44</b>
<b>TOTAL – LINE ITEM COST</b>	<b>32.43</b>	<b>37.82</b>

## Recommendations

- The creation of a Executive Committee of Cyclotron Center of Excellence in Guadalajara, with members representing public and private sector and Energy Life Sàrl, to explore the need for a national facility.
- Complete the current Business Plan with the information procured in the *country*.
- Considerable scientific and economic benefits are gained in using the 70 MeV cyclotron compared to use of the 30 MeV cyclotron in terms of the variety and quantity of isotopes that can be produced.
- Benefits derived from operation of a 70 MeV cyclotron instead of one at a lower energy are the ability to produce isotopes that cannot be produced at the lower energies.
- Despite the cost difference, which is not huge, scientific and economic benefits associated with the purchase and operation of a 70 MeV cyclotron, which are above the achievable with a cyclotron 30 MeV are substantial.

## Conclusions

The benefits of this facility will be greatly enhanced by leveraging existing isotope processing capabilities and by utilizing the existing experience.

The proposed radioisotope production facility based on a high-power will provide a full spectrum of capabilities for the production of isotopes for use in research, medicine, industry and Radiobiology as well as archeology and agriculture.

The Center will become a focal point in research activities and scientific collaborations, with the use of most advanced resources, and will increase the scientific, production, and educational value of the recommended accelerator facility.

With all the above, are undoubted benefits, it offers a system with a dual beam accelerator 30-70 MeV, for the Centre of Excellence. The calculations presented are based on past experience and Arronax and at BNL facility centers.

## References

1. IBA C70 CYCLOTRON DEVELOPMENT, Cyclotrons and Their Applications 2007, Eighteenth International Conference, L. Medeiros Romao, M. Abs, J-C. Amelia, W. Beeckman, J-L. Delvaux, Y. Jongen, W. Kleeven, Y. Paradis, D. Vandeplasse, S. Zaremba,, IBA, Chemin du Cyclotron 3, 1348 Louvain-la-Neuve, Belgium
2. COST/BENEFIT COMPARISON FOR 45 MEV AND 70 MEV CYCLOTRONS. Conducted for: U.S. Department of Energy, Office of Nuclear Energy, Science, and Technology Office of Nuclear Facilities Management, and Jupiter Technical Management Solutions, MAY 26, 2005
3. A Cyclotron Concept to Support Isotope Production for Science and Medical Applications, Brian J. Egle et al. Oak Ridge National Laboratory, 2008.
4. Construction and Operation of Cyclotrons for Medical Isotopes, Nigel Stevenson, TRIUMF.
5. Review of Cyclotrons for the Production of Radioactive Isotopes for Medical and Industrial Applications, Paul Schmor, Advanced Applied Physics Solutions, Inc. Canada.
6. European Nuclear Medicine/Radiopharmaceuticals & Stable Isotope market, MarketsandMarkets, 2013.