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Executive Summary

This document presents the final report of the Task3 - Work Package 4 - Innovation and Industries. It describes in particular the two subjects identified to offer GANIL an increase of its innovation potential in the future years: development of R&D and production programs for track-etched membranes, and development of electromagnetic isotopic separation activities.

1. INTRODUCTION

The Work Package 4 – Innovation and Industries – has focused on actions towards industrial users and on actions on industrial valorisation and innovation. They are of general interest as: access dedicated for industries for new applications to the existing GANIL accelerators and to the new SPIRAL2 facility, and proposal on involvement of industrial users within GANIL-SPIRAL2 organisation (Task1), general support for industrial valorisation and technology transfer (Task2), and study of the increase of innovation potential of GANIL-SPIRAL2 (Task3).

The objectives of Task 3 are to study the possibilities of increasing the innovation potential of the GANIL laboratory, with the following actions:

- Identify new applications to heavy and light ions beams, to replace the reactor technology with the accelerator technology, for as many applications as possible
- Identify new R&D subjects that might lead to innovative technologies and applications
- Identify the necessary technical developments to adapt the facility to these future and new applications.

This thematic is becoming more and more important in the national and international context, and the GANIL facility can offer, through its specificities and its various scientific and technical developments, a lot of new application fields and innovations.

2017 was dedicated to bibliography studies and brainstorming on new applications with the use of heavy and light ion beams (GANIL and SPIRAL2 facilities) and new fast neutron beams produced by the SPIRAL2 facility. Several application domains were identified: Boron Neutron Capture Therapy (BNCT), Neutrons for analysis and Neutron Activation Analysis, Production and separation of isotopes, Membranes and filtration by Nanostructuration with Middle and High Energy Ion Beams, Low Energy Focused Ion Beams. The medical radioisotope field is taking off, and this thematic is included in sub-task 2.4.

Two subjects were selected to be investigated in details in 2018:

- Membranes and filtration by nanostructuration with middle and high energy ion beams
- Production and separation of isotopes (other than for medical applications) by an electromagnetic process.

Both subjects are presented into details in this deliverable report, with detailed information allowing the next Ganil directorate (and its Steering Committee) to choose one (or both) of these technologies to be developed at GANIL, depending on the level of innovative activity they will aim to create.

2. TRACK-ETCHED MEMBRANES

2.1. INTRODUCTION ON THE STUDY CONDUCTED ON TRACK-ETCHED MEMBRANES AND GENERAL BACKGROUND

Membranes technology embraces the production of polymeric membranes (standard chemical composition of polymers includes carbon, oxygen, hydrogen and nitrogen atoms) via a technique called *track etching* or *swift heavy ion* irradiation which has been patented by Price and Walker in 1967 in General Electric (GE). The production process includes three subsequent steps: ion irradiation of a polymeric film (mostly polycarbonate – PC, polyethylene terephthalate - PET or polyimide - PI) with high-energy (mostly MeV range) heavy ions; chemical etching, and post-production treatment associated directly with the membrane's specific application. Track-etched membrane (TEMs) technology results in the manufacture of uniformly sized micro/nanoporous polymeric structures with channel-like pores (pore geometry: cylindrical, conical, funnel-like or cigar-like) induced by energetic ions, called lateral tracks, which are further revealed via chemical treatment under various conditions (e.g. elevated temperature, acids). Other possible TEM modifications include chemical functionalization, surface treatment, and sterilization process.

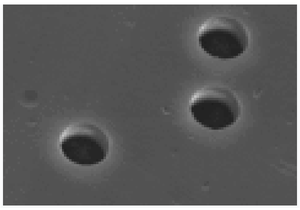

Figure 1. Etched Ion Tracks in the Polymeric Film (source: *wikipedia.com*)

The most recent technological advancement around the TEMs includes the utilization of the UV light (the technique is called *Track-UV*) for the sensitization (i.e. enhancement of particle tracks) of the polymeric structure. The use of the light within the UV range facilitates the creation of lateral tracks under irradiation by making the polymer more sensitive to the production process. Consequently, the UV light helps to diminish the requirements of the post-radiative track revealing treatment by making the polymeric film more reactive towards etchant. A similar sensitization effect can be also achieved via ozone treatment, solvent treatment of thermal treatment for certain types of polymers.

The TEMs characterization includes determination of the pore size distribution measured via a porometer and geometry/size of the pores, which are obtained by two complementary electron microscopy techniques: scanning electron microscopy (SEM) and high-resolution transmission electron microscopy. In the case of chemical functionalization, the Fourier-Transform Infrared Spectroscopy (FTIR) is used to determine the presence of functional groups.

A broad market study has been performed, which presents the international situation and all the applications using TEMs. This study shows some "niche" markets requiring the development of new types of TEM, with new materials and new functionalities. Ganil's potential for these future developments has been assessed, putting forward the facility specificities. A business plan based on these future activities has been developed and is presented in the deliverable D4.1 (cf. Task1).

2.2. GANIL's Potential Towards TEM Production

2.2.1. Description of the facility for Track-Etched Membrane Irradiation in GANIL

Irradiation of the polymeric film in GANIL's facility is undertaken using a special membrane dispenser system equipped with a set of rolls, which was initially built in 1987 (see Figure 3), and whose control system was renewed last year. A polymeric film is mounted on the stand with a rolling system followed by beam exposure in the air (Figure 2). The quality of the beam is precisely controlled via continuous monitoring of the ion flux parameters in the operation room (e.g. beam intensity or beam position).

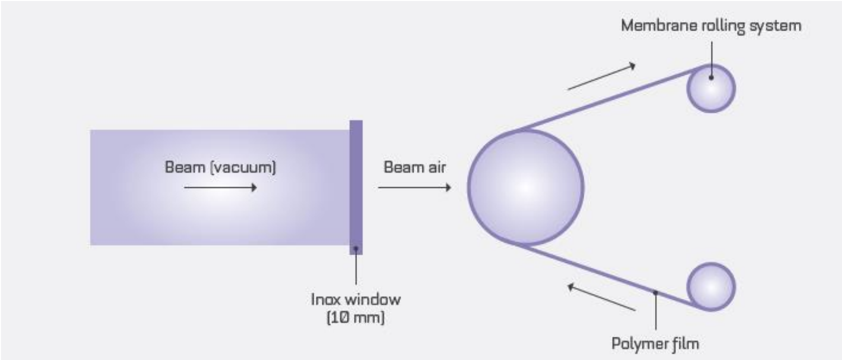

Figure 2. Scheme of the Membrane Production System

The TEMs produced at GANIL's facility are well-known for its high quality (e.g. well-defined pore structure) resulting from excellent beam stability, high irradiation spot precision, and high beam intensity. The table 1 below summarizes some technical aspects of the polymeric TEMs: initial film width and thickness, the pore density range, and estimated irradiation cost per square meter linked to the irradiation speed expressed in meters per minute. It is worth mentioning here, that the standard TEMs are not thicker than 50 microns which allows GANIL to irradiate either multiple layers of the polymeric film simultaneously or simply produce thicker films as compared to the commercial one.

Table 1. Membrane Production in GANIL – Selected Technical Specifications.

The maximum width of a roll (cm)	50
Thickness range for PET (µm)	20 – 125
Pore density range (pores per cm^2)	10^4 - 10^6 (low pore density) up to 10^9 (high pore density)
Irradiation cost (euro per m^2)*	0.31 (low pore density) – 124 (high pore density)
Irradiation speed (meters per minute)	0,25 – 100

**not including the 8 hours flat rate for beam tuning and pore density calibration (around 7440 €)*

Please note, that the final pore density is correlated with the effective beam intensity, degrader utilization (i.e. aluminum degrader), and irradiation speed/time. These parameters directly affect the final production cost (the higher the pore density the slower the sweeping beam irradiation of the film and consequently the higher production cost of TEM). Currently, the TEM irradiation is mostly performed using one cyclotron CSS1 (Krypton-78 beam; E = 10.5 MeV/A) intended for thin-film production. For the thick-film irradiation the combined heavy ion beam from cyclotrons CSS1 CSS2 (Lead-208 beam; E = 29 MeV/A) is used (e.g. Kapton/DuPont, thickness above 50 microns). The CSS1 beamline can be also replaced by a complementary use of of the CIME cyclotron (Krypton-78 beam; E = 10.5 MeV/A).

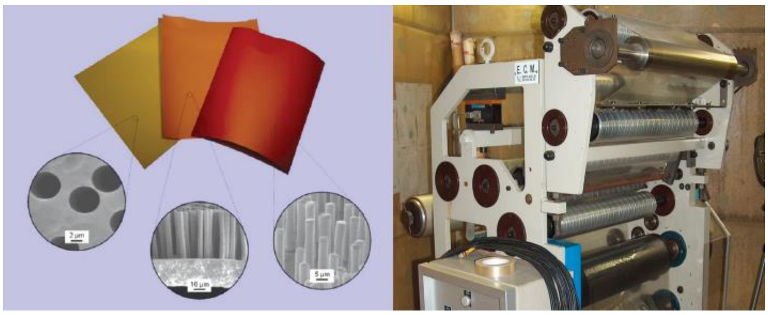

Figure 3. Microporous Membrane (left) and Membrane Dispenser System in GANIL (right)

The total cost of GANIL's operation was widely explored within the frame of WP3 Task 1 of the IDEAAL project and is presented in the deliverable D4.1.

2.2.2. GANIL vs. Other Nuclear Physics Laboratories

The global track-etched membrane market is currently saturated with the polymeric films produced in other countries worldwide (i.e. Belgium, Germany). However, GANIL has a range of advantages to compete with other facilities such: excellent beam stability, high beam reproducibility, beam irradiation spot precision, homogenous beam distribution (±5%), elevated beam intensity, high irradiation efficiency and wide energy range towards the production of thicker or more dense polymeric films. These qualities make GANIL's facility unique as compared to other nuclear physics laboratories. To support this statement, the table below (see Table 2) represents the list of facilities similar to GANIL where the TEM production takes place.

Table 2. Comparison of Various Nuclear Physics Laboratories Similar to GANIL.

Name of Facility	Location	Type of Accelerated Ions	Energy (per nucleon)
GANIL	Caen/France	Krypton-78 Lead-208	10.5 MeV/u 29 MeV/u
GSI/UNILAC	Darmstadt/Germany	from Hydrogen to Uranium	2 - 11.4 MeV/u
RIKEN/RILAC	Saitama/Japan	Xenon-136 Uranium-238	up to 680 keV/u
JINR/SHEF	Dubna/Russia	from Helium to Uranium	4 - 8 MeV/u
TSL	Uppsala/Sweden	Xenon-136	8.3 MeV/u
CERN/LINAC 3	Geneva/Switzerland	Lead-208	4.2 MeV/u
CDR/CYCLONE	Louvain-la-Neuve/Belgium	Xenon-136	up to 6 MeV/u
NSCL/K1200	East Lansing/USA	from Oxygen to Uranium	8 - 80 MeV/u
TRIUMF/ISAC	Vancouver/Canada	from Helium to Calcium	5 - 11 MeV/u

Compared to other places in Europe, GANIL has an added value (higher energy beam range allowing for deeper high LET ion penetration) making it a competitive place with a wider range of possibilities towards TEM production. The main competitors of GANIL in Europe are the GSI, the TSL, and the CYCLONE facilities in Germany, Sweden, and Belgium, respectively. On a commercial level, the polymeric TEMs are irradiated using mostly the Krypton and Xenon beam. The energy of the heavy-ion beam affects the efficiency of the ion penetration through the polymeric film making low energy beam (up to 11 MeV per nucleon) only applicable to certain types of polymer while limiting their maximum thickness (e.g. less dense materials, like PC or PET, with a maximum thickness of 50 microns). In consequence, low energy beam efficiency requires the irradiation of TEMs to take place under a vacuum atmosphere which increase the beam efficiency towards better energy deposition and avoids an additional window.

In contrast, GANIL has a higher energy beam for heavy ions (up to 30 MeV per nucleon) with more effective beam penetration (high LET beams like ^{208}Pb). In GANIL polymeric TEM irradiation can be performed under the air atmosphere (beam energy high enough to cross a thin stainless-steel window) without compromising on their thickness nor the initial material structure and physicochemical characteristics. This makes the GANIL's facility very unique among others allowing to produce polymeric films as thick as 120 microns.

Up-to-date, the most robust and challenging polymer to produce on the market via TE technology is the Polyimides (PI - commercially introduced by the iIT4IP company from Belgium). The PI production with a maximum thickness of 50 microns is currently performed in the GSI facility using the Xenon beam (^{129}Xe; E = 5 MeV per nucleon) under vacuum. However, the beam irradiation of thicker PI polymeric film requires significantly higher energy heavy ions and is not accessible in other places in Europe than GANIL in France. The most common polymers, such as Poly Carbonates (PC) or Polyethylene terephthalate (PET) films, can be produced via a lower energy beam (e.g. Krypton, Xenon, Argon, Neon) making the common TEM technology only applicable to a certain type of polymeric materials. The PI polymer can be also functionalized via radical under controlled atmosphere (e.g. helium gas).

Irradiation of fluorinated polymers, such as PVDF or PTFE, remains challenging on the commercial level due to higher material density (i.e. semi-crystalline structure) and chemical inertness. However, those polymers possess unique properties (e.g. PVDF – piezoelectricity, dielectricity). Consequently, their production via TE technology requires to increase significantly the efficiency of the swift heavy ion beam penetration (i.e. high energy heavy-ion beam) through their structure. In addition to that, the fluorinated polymers are also chemically inert so the chemical etching step is more challenging as compared to PC and PET (e.g. corrosive, dangerous solutions of potassium/magnesium are needed to open the pores.

It appears that the technology of the thick film/fluorinated polymer produced by track-etching is currently not accessible in Europe, opening many doors to GANIL for future development. The most promising ones include the production of high-performance fluorinated polymers (e.g. PVDF, PTFE) or thick polymeric films (e.g. PI above 50 microns) which are suitable for more demanding operating conditions (e.g. high temperature or acid environment) than commercial engineering thermoplastics (e.g. PC or PET). Many new and future applications of such polymers have been identified during this study, by analyzing scientific publications, filed patents and new commercial products. One of the very last development was made at GSI in 2020 for fast, highly sensitive, and selective SARS-CoV-2 detection with single nanopore TEMs as a sensor, and was published by GSI/FAIR group working together with international partners

2.3. Market Studies

Production of polymeric membranes via track-etched technology together with GANIL's capability to do so requires knowing the 'big picture' of the TEMs global markets. To make informed decisions regarding the GANIL's future activity towards possible TEMs production and its commercialization the author examined three potential global markets to enter:

- Track-etched membrane global market
- Microfiltration global market (pore size = 0.02 - 10 µm)
- Ultrafiltration global market (pore size = 0.001 - 0.02 µm)

The first track-etched membrane global market is described profoundly due to its high relevancy (production method, type of polymeric material, etc.). The other two markets listed above (microfiltration and nanofiltration global markets) were selected only for the comparative purpose as well as an alternative potential market to be considered. Since membranes present on those markets either are made of polymeric material or are produced via track-etched technology (e.g. PC, PET, and PI) hence the choice of those markets seems logical. Moreover, the pore size required for the micro- and ultra-filtration purposes corresponds to the one of TEMs currently produced and commercially available. Taking into account all of the parameters: pore size, geometry, type of polymeric material and the track-etched production technology, the TEMs are widely used for general filtration-related applications.

Lastly, to complete the 'big picture' around the technological trends it was also looked at the dynamic of the research work such as a number of scientific publications and intellectual property (IP) development worldwide.

2.3.1. Track-Etched Membrane Global Market

The track-etched membrane global market is predicted to reach 813.1 mln USD by 2023 from 476.0 mln USD in 2018, at a Compound Annual Growth Rate (CAGR) in percentage equal to 11.3%. In 2017, the global market size was equal to 428.4 mln USD, as shown in Table 3.

Table 3. Track-Etched Membrane Global Market Prediction in USD between 2017 and 2023.

	2017	2018	2023	CAGR(%)
Market size (USD)	428.4 mln	476.0 mln	813.1 mln	11.3

This increase of the global size market relates to increasing customer demand for the final product leading to the progressive development of the track-etched technology. The reason for such market dynamics depends on the three main factors: market drivers, market constraints, and opportunities. The main global market drivers include:

- increasing R&D spending in pharmaceutical and biopharmaceutical industries
- raising TEMs applications in nanotechnology
- increased purity requirements in end-user applications.

In terms of the global market restrains the relatively high production cost results in a limited supply of TEM products. However, from the future application point of view, the main market opportunity appears to be an ultrafiltration track-etched polymeric membrane market. The global track-etched membrane market is segmented into North America, Europe, Asia-Pacific (APAC), and Rest of the World (RoW). The higher share of the market is dominated by the North America region (both in supply and demand side). The second-largest share of the market is assigned to Europe followed by APAC and RoW. (Table 4)

Table 4. Market Share by Region (%) given for Supply and Demand Side.

Region	Supply Side	Demand Side
North America	41	37
Europe	22	24
Asia-Pacific (APAC)	20	22
Rest of the World (RoW)	17	17
Total	**100**	**100**

Several facilities in Europe (including Ganil in France) makes Europe (22% and 24% of the global market share for supply and demand side, respectively) the main region of interest regarding the possibility to enter the global market. Europe holds nearly one quarter of the global market share so the attractiveness of the regional market is already high for both the production and demand side. Unfortunately, the data for the French regional TEMs market was not accessible.

Another type of market segmentation includes potential end-user application of the TEM technology. The TEMs found their main utility in Pharmaceutical and Biopharmaceutical Companies (42%), Academic & Research Institutes (28%), Food & Beverage Companies (15%), Hospital & Diagnostic Laboratories (10%), and Other End Users applications (5%) as presented in Figure 4.

Figure 4. Market Share by End User (%)

The Pharmaceutical and Biopharmaceutical Industries are the largest end-users of the polymeric membranes produced via track-etched technology. The reason for that is also aligned with the main market driver related to the growing R&D spending for research towards the development of biological molecules and manufacturing of the generic drugs.

Other types of market segmentation methods include the type of the final product (membrane filters, cartridge & capsule filters, other track-etched membrane products) and type of polymeric material (polycarbonate – PC, polyethylene terephthalate – PET, and polyimide - PI) used for the TEMs production. In these cases, the highest global market share belongs to membrane filters and PC-TEMs.

2.3.2. Competitive Landscape

As concluded in the previous part, the highest share of the global market belongs to North America (41%) and Europe (22%). Following that, an analysis of the competitive landscape in terms of companies currently producing or distributing the TEMs globally was realised. The aim was to establish the level of shared knowledge, a saturation of the market but also possible similarities between the companies in terms of production line of TEMs offered, as presented in Table 5.

Table 5. Key Market Players on the Global Track-Etched Membrane Market
North America (grey) and Europe (blue).

North America	**Foundation Year**	**Europe**	**Foundation Year**
GE Healthcare	1892	Merck Group	1891
Danaher Corporation	1969	it4ip S.A.	2006
Corning, Inc.	1851	Oxyphen AG	1953
Sterlitech Corporation	2001	Brand GmbH & Co KG	1949
Sarstedt AG & Co. KG	1961	Sartorius AG	1870
Zefon International, Inc.	1990	SABEU GmbH & Co. KG	1958
Thermo Fisher Scientific	2006	GVS S.p.A.	1949
Avanti Polar Lipids, Inc.	1969	Eaton Corporation, Inc.	1911
SKC, Inc.	1976	Greiner Bio-One GmbH	1868
Graver Technologies LLC	1866	Machery-Nagel GmbH & Co. KG	1911

Simply by looking at the names of the companies/year of foundation, the global TEMs market appears to be mature, highly competitive, and saturated with this type of technology. To go a bit deeper with this analysis it was looked also for similarities between companies (see Table 6) including the type of polymer, surface properties or surface coating, method of sterilization, format, pore size, and lastly commercial price (in euro) of TEMs.

The high number of key market players, their long presence on the global market, and hence the maturity of the market show high entry barriers for GANIL to be competitive. Moreover, a high level of similarity between the companies' product range also indicates no need for high-volume production of TEMs in none of the possible application domains.

Based on the main market driver (R&D research development) and high CAGR%, it is suggested to use the competitive advantage of GANIL and its added-value (i.e. beam stability, high energy range, heavy ions, beam intensity) for further exploration of any potential niche market where a small volume of TEMs are sold at a high price.

Table 6. Summary of the Most Common Properties of the Commercially Produced Polymeric TEMs.

Type of polymer	polycarbonate (PC), polyester (PET), and polyimide (PI)
Surface properties	hydrophobic or hydrophilic (PVP coating)
Surface coating	metal coated (Ag, Au, Cu, Al or Ti), dyes
Sterilization	autoclave (30 min at 120 °C), ethylene oxide (EtO) or gamma-rays
Format	rolls, flat sheets, discs, square or rectangular shape, customized
Pore size range	0.01 - 30 µm
Thickness range	6 - 50 µm
Price range for the end product	producer/pore size/diameter/material/configuration/quantity dependent Example: 56,63€ - 186,00€ (for PC, diam. 13-47, pore size 0.1 - 12 µm, pack of 100)

2.3.3. Microfiltration and Ultrafiltration Global Market

The other two possible markets to enter include microfiltration and ultrafiltration global markets where polymeric membranes can be used for general filtration purposes due to the pore size range offered by track-etched technology. In this part the size of the market and its CAGR% are analyzed to see whether those markets could be of potential interest for GANIL (Table 7). The market estimation given in this section should represent the finale "sale price", however, the market size of membrane irradiation should be an order of magnitude lower.

Table 7. Microfiltration (blue) and Ultrafiltration (green) Global Market Predicted Compound Annual Growth Rate (CAGR%) and Market Size between 2017 and 2023, given in USD.

Global Market		2017	2018	2023	CAGR(%)
Microfiltration	Market size (USD)	2.2 billion	2.4 billion	3.7 billion	9.0
		2015	**2015**	**2021**	**CAGR(%)**
Ultrafiltration	Market size (USD)	3.1 billion	3.2 billion	4.6 billion	6.9

The track-etched global market presented in section 2.3.1 has its CAGR equal to 11.3% as measured between 2018 and 2023 whereas the size market is predicted to reach 813.1 mln USD by 2023 from 476.0 mln USD in 2018. In the following cases, the CAGR between 2018 and 2023 of microfiltration and ultrafiltration global markets are 9.0% and 6.9%, respectively, which is nearly 2.3% and 4.4% lower compared to the track-etched membrane global market. However, both of them are still in a development stage opening the possibility for GANIL to enter those markets. In terms of the size, microfiltration and ultrafiltration global markets were estimated to be 2.2 billion and 3.1 billion USD, respectively, as measured in 2017. The prediction for 2023 estimates them to reach a size of 3.7 billion and 4.6 billion for microfiltration and ultrafiltration global markets, respectively, which is 1.3 billion and 1.4 billion higher compared to 2018.

Finally, the polymeric track-etched membranes currently present on the microfiltration and ultrafiltration global market are mostly used in the following applications:

- biotech/biopharma/pharmaceuticals
- medical (hemodialysis)
- industrial processes
- food and beverage
- potable water and wastewater treatment
- semiconductors (purification)

The first application segment also corresponds to the main commercial end-user identified in the track-etched global market membrane described at the beginning of this chapter.

2.3.4. Scientific Publications

Scientific publications and intellectual property (IP) represent global trends in the research and development of the TEMs technology and potential direction of future market needs. Understanding the technological need and environment is crucial to decide about the direction of potential GANIL's TEM production.

The TEMs commercially available are mostly made of polymers such as PC, PET, or PI. Apart from the popular polymeric membranes, polytetrafluoroethylene (PTFE) and polyvinylidene fluoride (PVDF) are also of high interest due to their unique properties (e.g. piezoelectricity – PVDF, dielectric properties – PTFE). In the following study (Table 8), two complementary search engines, namely Web of Science and Scopus, were used to check the number of scientific publications dealing with the most common polymeric membranes produced via track-etched technology.

Table 8. The total number of scientific publications for various polymeric TEMs from 2008 to 2018 according to Web of Science and Scopus search engines (highlighted - PC, PET, and PI are commercialized; PTFE and PVDF are not available on the commercial market).

Type of Polymeric Track-Etched Membrane	Web of Science	Scopus
Polycarbonate (PC)	243	249
Polyethylene terephthalate (PET)	106	112
Poly(ether)imide (PI , also PEI)	13	9
Polytetrafluoroethylene (PTFE)	16	9
Polyvinylidene fluoride (PVDF)	10	6
Total	**388**	**385**

Table 8 shows that both search engines employed in the study give similar results regarding the total number of publications for each type of polymeric TEM. The main scientific work focuses on the utilization of PC and PET polymers (average number of publications: 246 and 109 for PC and PET, respectively), which are commercially available at high volume on the market. In terms of PI, significantly lower (average number of publications: 11) number of publications directly reflects the commercial volume of the product. For the last two types of polymers, PTFE and PVDF (average number of publications: 16 and 8 for PTFE and PVDF, respectively), the R&D interest is comparable to the commercial PI membrane

Figure 5. Sum of times the scientific paper is cited by year as shown for five types of track-etched polymeric membranes (PC – light blue, PET – orange, PI – grey, PTFE – yellow, PVDF – dark blue)

Lastly, the global trend around the R&D work can be visualized as a sum of times cited each year (Figure 5). Looking at the figure it can be concluded that commercially available PC, PET, and PI track-etched membranes experienced on average a steady increase around the R&D work. Apart from the small decrease observed in 2014, 2016 (PET), and 2017 (PC, PI) research activity in the topic of polymeric TEMs is still in the development stage. The highest interests are shown for the PC and PET made TEMs, however, the most promising future polymeric material seems to be PTFE. Compared to other types of polymeric TEMs, the PVDF shows the lowest level of R&D interest with no significant increase over the last 10 years.

2.3.5. Intellectual Property (IP)

The information regarding the IP development for TEM technology has been collected based on Orbit Innovation software developed by the *Questel* Consulting Company. The total number of active patents (active means that the license is currently paid by the patent owner) for various types of polymeric membranes (PC, PET, PI, PTFE, and PVDF) has been taken into account and analyzed towards global trend representing the technology development over the last 10 years (between 2008 and 2018). The patent deposition process takes up to 18 months, which explains why the analysis is done only until 2017. Moreover, the total number of patents for TEM does not represent a sum of patents for each type for polymer simply. The reason for that is that each patent can include other types of polymers as well which can be used for certain technology. The results are represented in Table 9.

Table 9. Total Number of active patents for the TEM technology for different types of polymers (PC, PET, and PI are commercialized; PTFE and PVDF are not commercialized).

Type of Polymeric Track-Etched Membrane	Number of Active Patents
Polycarbonate (PC)	387
Polyethylene terephthalate (PET)	143
Poly(ether)imide (PI , also PEI)	139
Polytetrafluoroethylene (PTFE)	111
Polyvinylidene fluoride (PVDF)	69
Total	**565**

The number of active patents worldwide for the polymeric TEM is 565 with the highest number of deposited patents using the commercial PC membrane (number of patents = 387). However, nearly 2.7 times fewer patents are registered for the PET polymer (143 patents), which is the second most popular type of material. The third and fourth position is taken by PI and PTFE (number of patents = 139, and 111, respectively) followed by the last position occupied by the PVDF polymeric TEM (69 of active patents). Such a trend is in agreement with the previous results related to the number of publications mentioning each type of polymer. The number of patents, however, does not show the general trend linked to technological development that is why the number of active patents per year (from 2008 to 2018) has been plotted versus the type of polymer used to produce the TEM (Figure 6).
The TEM technology (blue line) shows a progressive increase of investment up to 2017 (increase by a factor of 2) with two small declines in 2008 and 2016, respectively, as compared to 2007. The most popular type of polymer is the PC (red line) with an investor increase by a factor of 2.5 between 2007 and 2017 with 2 significant declines in 2014 and 2016. However, the overall trend for PC-TEM represents the constant development of technology. The shape of the PC curve follows the same trend as the total TEM patents (blue) because most of the patents use commercially available PC membranes produced in a high market volume. The other types of polymers have significantly lower interest compared with the PC. The PET shows an increase by a factor of 2.1 up to 2017 with two the highest number of active patents in 2015 (23 patents) and 2016 (20 patents), respectively. A similar situation is observed also for the PI-TEM (increase by a factor of 1.4 between 2007 and 2017). The highest growth is noticed for the PTFE membrane by a factor 6. The lowest number of active patents mention the PVDF polymer as a TEM material, however, the increase is also noticeable (by a factor of 4.0 between 2008 and 2017 whereas in 2007 any patent for the PVDF-TEM was deposited).

Figure 6. Development of the TEM technology based on active patent deposition (blue – total number of patents) for various types of polymers (PC - red, PET - green, PI - purple, PVDF - blue, and PTFE - orange) between 2007 and 2017.

In conclusion, the investment in TEM technology has been progressively increasing over the last 10 years. The higher number of paid patents uses commercial PC polymer, however, other types of materials (e.g. PET, PI, PVDF, and PTFE) has also been gaining some interest (a steady growth is observed).

To complete the previous information, a test with a new innovative software called *Orbit Innovation* (by *Questel*) could be performed. This business-oriented software is a powerful patent search engine with a full analytical tool covering the entire IP needs across the innovation lifecycle with a full financial analysis. In short, it appears that polymeric TEM technology is heavily invested around the world with an increase of more than 30% observed between 2014 and 2017. The main patent activity belongs to China, the US, and Japan followed by European countries (i.e. Germany, France, and Finland). Chemical technology and biotechnology are of the main fields of interest for the investors with R&D labs being the most popular end-user of the TEM technology.

2.4. Applications & Perspectives

The TEM applications have been studied using primary and secondary sources of information. The primary source includes direct access to scientific publications and intellectual property (i.e. patents) database, internet websites of commercial TEM producers or distributors, and last but not least, the Wikipedia website. The secondary source of information is based on interviews with scientists and people either experienced or currently working with the TEM technology. This approach revealed many possible TEM applications that are either in the development stage (i.e. extensive R&D is being conducted) or could potentially meet the future market needs (e.g. niche applications).

The study revealed that the polymeric TEMs have been used for various applications in a wide range of domains (Figure 7). Moreover, their unique structure qualify them as a '360°-application range' material with many areas of interest that are not commercially addressed making the global TEM market open for new ideas and innovative technologies.

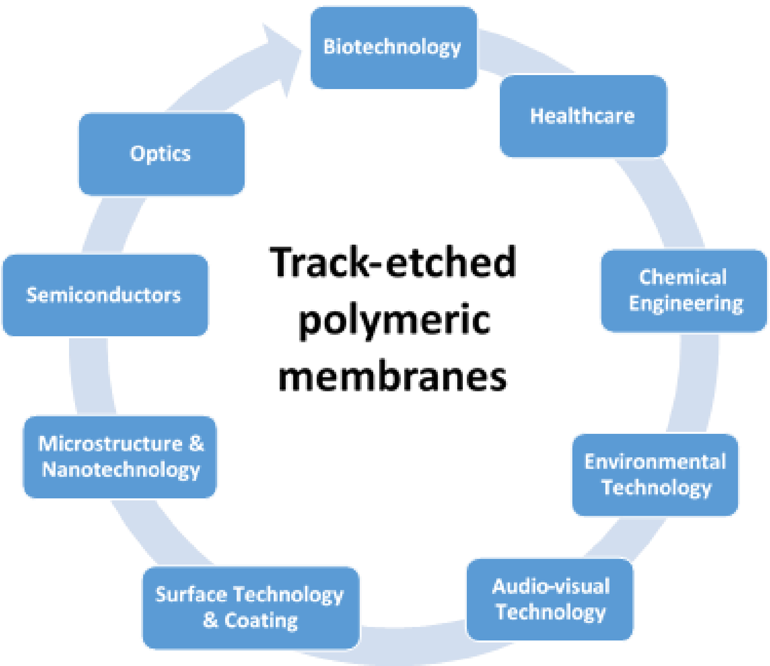

Figure 7. Main Application Domains of Track-Etched Membranes.

The list seems to be endless with many possible applications that could be potentially addressed by GANIL. The competitive advantage of GANIL towards TEM production could potentially target all applications requiring the use either thicker (above 50 microns) or denser polymers with better mechanical/thermal properties (e.g. polymers operating in elevated temperatures or corrosive/acidic conditions). The examples also include fluorinated polymers (e.g. PVDF or PTFE) or polymers with imide-groups (e.g. Kapton as a trademark of DuPont where an initial polymeric material is a polyimide - PI) allowing to expand the market above the well-established and commercially available polymers (e.g. PC and PET).

Up-to-date, the most common TEM applications are within the healthcare area (e.g. cancerology, cell biology, and blood filtration). The other promising sectors involve automotive (e.g. fuel cells), aerospace (e.g. ventilation), energy (e.g. blue energy generation), and electronic (e.g. soft electronics) industries. An exhaustive list of current TEM applications along with the most promising ideas suitable for further exploration of untapped markets has been established.

2.5. Business Models & Business Plan

The GANIL facility has an added advantage towards entering the track-etched membrane (TEM) global market. More specifically, competitive benefits include:

- High beam stability
- Online and precise beam monitoring
- A large variety of available ions (light to heavy ions)
- Wide energy range (up to high energy 29 MeV/A for Pb beams)
- Wider range of material types and thicknesses to be irradiated, compared to other similar facilities

The global market analysis showed many current and potential future applications of the TEM technology in various domains, e.g. healthcare, energy, environment, and electronics, just to name a few. However, up-to-date none of these domains expresses a need for a high volume of TEMs that GANIL can deliver. In order to maintain GANIL's sustainability and progressive development of its activity around ion track-etched technology, three possible business models can be proposed:

- BM1: Increase of Commercial Visibility of GANIL Towards the Production of Track-Etched Membranes
- BM2: Contract(s) with an Existing Company
- BM3: R&D Project + Startup Company

These three business models are presented into details in the deliverable D4.1.

2.6. Conclusion on the track-etched membrane activity

The TEM global market is mature, saturated, and very competitive with R&D / IP constantly developing, heavily invested, and possibly very profitable. Companies compete on the market by reducing their price margin, developing or acquiring a new technology, expanding regionally or by offering a complete market solution. High market competition results in high entry barriers for new potential market players like GANIL.

In the current state, GANIL cannot compete with current commercial TEM producers by selling common types of raw polymeric films (e.g. PC, PET, or PI) with similar physicochemical properties (e.g. thickness). GANIL can compete on the TEM market by means of the dense polymeric film (e.g. PTFE or PVDF) and their thickness range (i.e. thicker materials or even multi-layer, simultaneous film irradiation). The added value of GANIL (highly energetic, stable heavy ion beam) is of commercial importance with potential high market value which can be used for further development of TEM technology.

To enter the market, GANIL associated to a chemistry laboratory, can increase its level of expertise towards a positioning on R&D on full production process for innovative material, in collaboration with a laboratory expert in chemical treatment (e.g. beam irradiation/chemical etching/functionalization/material characterization). Higher level of GANIL/chemistry laboratory expertise together with an innovative idea or niche TEM application may result in the opening of a new, untapped market and development of novel end-user products.

Up-to-date, one application with breakthrough technology has not been found but a high volume market (e.g. automotive, healthcare) has been detected, and the corresponding Business Model 3 (R&D + Startup) has been defined (cf. Deliverable D4.1)

The GANIL facility has a potential for high-volume production to address the potential market, however, to break the entry barriers GANIL must use the competitive advantage to differentiate from TEMs commercially produce elsewhere. Moreover, existing infrastructure in GANIL (i.e. ready-to-use membrane dispenser system) reduces the initial investment cost, and a Business Model based on the R&D activity and the startup allowing exploring potential market opportunities as well as testing the need of the market by offering the free TEMs sample is adapted. Assuming that a niche and profitable market exists, the free TEM samples produced in GANIL could help to ease the identification process of a commercial market thanks to the analysis of the customers' profile. From the classical business model point of view, the startup could also take action towards market exploration (i.e. hidden market or new, untapped market). Contacting companies with potential interest in R&D development of polymeric TEMs which are in line with their commercial products can open new opportunities (e.g. full TEM-based device or other TEMs products). The main advantage of this model is lower investment risk as well as further exploration of the market towards new applications tapping the competitive advantage of GANIL. The current market has high entry barriers with a high level of expertise and maturity across the market players, both in Europe as well as worldwide.

3. Electromagnetic Isotopic Separation

3.1. Introduction

As far as production and separation of isotopes by an electromagnetic process are concerned, the study has been conducted on three main points:

- a complete market study and assessment of the international situation, from which the necessity for an organized network at the European level appears
- the assessment of the added value of the Ganil facility in this domain, and in particular the identification of isotopes which could take advantage of it
- a proposal for R&D actions at GANIL, upstream a phase of valorization.

3.1.1. Methodology

The methodological approach applied to fulfill the Task3 main objective for the isotope subject includes the following steps:

- An extensive study of the literature to understand the isotope separation technology development, current trends, and the type of isotopes separated by each of them. The review focuses on basic principles of currently employed and novel techniques including their advantages, limitations, and possible solutions to address them.
- Revision of the global isotope market for both stable and radioactive elements including current market situation, isotope pricing policy, novel trends in research development, and future of the technology. The market studies are based on market research resources (i.e., BCC Research) and open-source reports published by experts and world-leading organizations (e.g., Nuclear Physics European Collaboration Committee - NuPECC; Department of Energy – DOE; and The Russian Federal Atomic Energy Agency – ROSATOM). The general situation within the isotope production, distribution, and R&D is presented followed by extraction of isotopes in-high global demand, in short supply, or under development.
- Internal and external interviews with resource persons to define the GANIL's added value. This part includes an analysis of GANIL's situation, ongoing/future projects, and activities around isotopes followed by mapping of the strengths and the most promising aspects of GANIL. The interviews also resulted in a list of isotopes defined as potential candidates for separation in GANIL. The combination of the list with the current/future market needs leading to the extraction of the potential isotopes of interest followed by further study of their technical aspects towards separation in GANIL.
- Summary of all findings has been shown to GANIL's direction to obtain their opinion about the conducted work resulting in final conclusions and recommendations for future actions. The most optimal direction of the GANIL facility towards isotope separation activity has been defined.

3.1.2. General Background

Isotope is an atom of the same element with the same number of protons in the nucleus, or the same atomic number (Z), but with a different number of neutrons (N) in the nucleus, or different atomic weights (A), expressed as a sum of protons and neutrons). As the mass of the proton and neutron is very similar (1.672623×10^{-27} kg vs. 1.674929×10^{-27} kg, respectively), the isotopic stability is mainly determined by the neutron-proton ratio (N/Z) of the atomic nuclei were both are attracted to each other by the nuclear force. For larger nucleons, the nuclear force decreases exponentially with distance. Consequently, the N/Z ratio and size of the nucleus divides isotopes into two groups: stable/non-radio-active and unstable/radio-active elements. Elements with an equal number of protons and neutrons are more likely to be stable (e.g., Carbon-12 with 6 neutrons and 6 protons; N/Z = 1). The highest N/Z ratio of stable nuclei for the isotope of uranium is 1.587 (i.e., Uranium-238 with 92 protons and 146 neutrons). The radio-active elements generally decay into stable ones via alpha (especially true for heavy nuclei or neutron deficient), beta (excess of neutrons) decay, or positron emission/electron capture (neutron deficiency). Radio-active isotopes decay into other elements within a certain time period called half-life ($T_{1/2}$). Another factor often recalled for isotopes is their natural abundance (i.e. a percentage of atoms with a specific atomic mass found on a planet) which can be determined using mass spectrometry (MS). As an example presented in Table 10, carbon has 15 known isotopes including 2 stable (C-12 and C-13) and one radio-active (C-14) element that can be found naturally on earth. The rest of them are synthetic with the longest $T_{1/2}$ of ~20 minutes given for Carbon-11.

Table 10. Main Isotopes of Carbon (source: *wikipedia.com*)

Isotope	Number of protons (Z)	Number of neutrons (N)	Atomic weight (A)	Stability/Half-life ($T_{1/2}$)	Abundance
Carbon-11	6	5	11	unstable/20 minutes	synthetic
Carbon-12	6	6	12	stable	98.9%
Carbon-13	6	7	13	stable	1.1%
Carbon-14	6	8	14	unstable/5730 years	1 ppt*

**ppt = parts per trillion*

Properties of certain isotopes determine their main applications which are used in a wide range of areas including:

- medicine
- energy
- basic research
- national security
- many others, just to name a few.

Often stable isotopes are precursors for the production of radio-isotopes. For example, Nickel-62 (a stable metallic element) when exposed to the High-Flux Isotope Reactor (HFIR) results in the production of Nickel-63 (unstable, beta-emitter with $T_{1/2}$ = 100 years) via neutron capture, Nickel-63 being commonly used in national security for explosive trace detection (ETC) technology. Similar to Nickel-62, neutron-based modification of Neodymium-146 results in the radioactive Promethium-147 (beta emitter $T_{1/2}$ = 2.6234 years) used in nuclear batteries (RIMS – Radioisotope Micro-power Source in advanced energy field) where beta particles are converted into electric current. Medical isotopes include popular radioactive Lutetium-177 produced via neutron irradiation of Lutetium-176. This medium-energy beta-emitter with a $T_{1/2}$ of 6.7 days and maximum energy of 0.5 MeV is used in modern medicine for cancer treatment due to maximum soft-tissue penetration of 2 mm. Modification of stable Gallium-69 with proton beam gives radio-active Gallium-68, known as PET imaging agent, with a positron-emission property and a half-life of 68 minutes. A summary of the main applications with isotopes in presented in Figure 10.

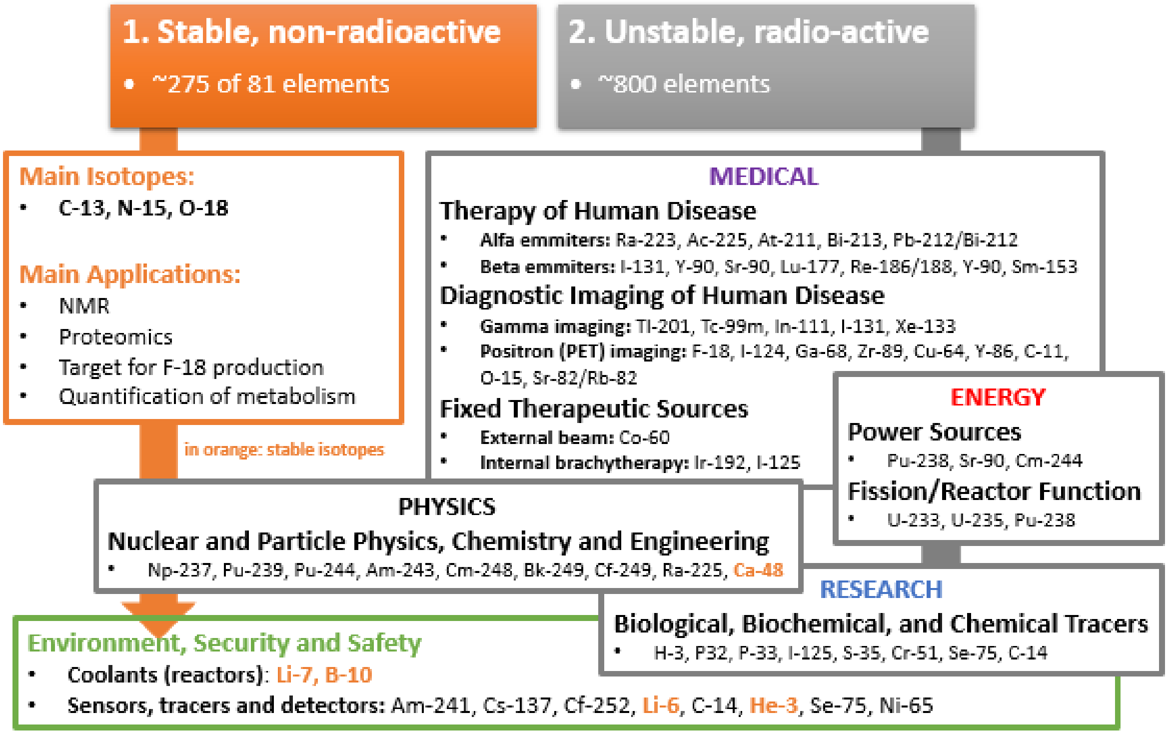

Figure 8. Summary of Main Isotope Applications

The list of possible applications seems limitless due to a high number of isotopic elements and versatile production methods. However, stable isotopes with low natural abundance or production of synthetic elements often require the employment of certain separation technology to extract the element of interest. That's why, the separation technology may also increase the isotopic purity which then determines their final application and its working efficiency (e.g., medical isotopes are ultra-pure).

3.2. Electromagnetic Isotope Separation Technology

In nature, most isotopic elements are found as a mixture of several isotopes with different abundance proportions. However, it is often favorable to separate only one isotope of interest from the others for certain applications (e.g., science, medicine, or industry). This process is known as isotope separation and allows to fractionate different elements within the mixture often leading to their natural enrichment. In the latter case, the enrichment process increases the concentration of isotope above its natural abundance. Historically, the separation technique was intended to obtain/isolate pure uranium-235 (^{235}U) from the mixture of ^{235}U (natural abundance = 0.71%) with uranium-238 (^{238}U) with a natural abundance of 99%. The enrichment process attracted world attention when humanity discovered how to use one kilogram of pure ^{235}U to build an atomic weapon during the Second World War. The extensive work on separation techniques was conducted simultaneously in the USA and Germany resulting in the development of various methods to extract the isotope of interest. The ultra-centrifugation, diffusion across thermal or osmotic pressure barriers, and deflection in the electromagnetic field were the techniques based on some small differences in the physical (i.e. mass) or chemical (i.e., chemical reaction rate) properties of the isotopes of a certain element. However, back in time many of those newly invented methods were unwieldy, inefficient, and expensive but developed out of necessity. The currently used isotope separation techniques are:

- Electromagnetic separation (EMIS)
- Gas Diffusion (GD)
- Gas Centrifuges (GC)

- Thermal Diffusion (TD)
- Distillation Fractional Distillation (FD) / Cryogenic Distillation (CD)
- Chemical Exchange (CE)
- Plasma separation (PS)
- Laser Separation (SP)
- Novel technologies

Electromagnetic separation (EMIS) is described, and a summary of the other techniques with their fields of applications is presented.

3.2.1. *Electromagnetic Enrichment and Purification*

The principle of Electromagnetic Isotope Separation (EMIS) to solve the isotope separation problem is similar to the one of the Mass Spectrometer (MS) invented by J.J. Thomson in 1907. As in other popular methods based on the physical difference in mass, the isotopes are transformed into ions via vaporization followed by acceleration in the electric field into extraordinary high speeds. In the final step magnetic field exerts a force on the accelerated ions and separation takes place based on their mass-to-charge ratio. The ionized particles in the magnetic field follow a circular trajectory and are separated in collectors or collector pockets. The EMIS method has been widely used for purification and enrichment of isotopes giving the purest material as compared to other methods.

The EMIS method was invented in the 1940s in the US and Russia as a part of the Manhattan Project and the Soviet Atomic Project, respectively, for the separation of heavy elements such as uranium (UF_6) and plutonium ($PuCl_3$). A special mass spectrometer machine, historically called calutron, was initially designed and build for the atomic bomb purpose but resulted in the separation of nearly every element in the periodic table.

Figure 9. Electromagnetic Separation: Basic Principle (right) of Uranium Enrichement (right)

Versatility of this method can yield some of the highest purities of the samples as compared to other techniques but low-throughput is quite costly and the last calutron in the US was stopped in 1998 due to high maintenance/operation cost. Nowadays, the EMIS technology is used for the separation of Tl, Pd, Sr, Ca, and the lanthanide series or in conjunction with other techniques to increase the overall isotopic purity.

Pros: ultra-high purity (> 94%), versatility and high selectivity
Cons: low production volume, high energy consumption, high production cost, low enrichment efficiency.

3.2.2. *Summary of the other techniques for isotopic separation*

Light, stable elements are well-separated by distillation, chemical exchange, or thermal diffusion by the private sector in metric ton range. Heavier isotopes require the employment of electromagnetic method (i.e., calutrons), gas centrifuge, or gaseous diffusion. Medium-level enrichment of heavier isotopes is also obtained by plasma separation whereas versatile technology of laser separation is limited to stable isotopes with gram/kilogram output volume. Nowadays, the most universal method used to separate grams of nearly every element in the periodic is electromagnetic separation resulting in the highest purity grade. Combination of two technologies (i.e., magnetic with laser or centrifuge) are also observed towards better performance and economic viability.

Table 11. Summary of Technologies Used For Separation of Isotopes

Separation Technology	Type of Isotopic Element	Output Volume	Example of Separated Isotopes
Electromagnetic	universal/heavier isotopes	grams	Tl, Pd, Sr, Ca, rare-earth, alkaline-earth, alkaline (25-30 elements), the lanthanides
Gas Diffusion	light isotopes	tons	C-13, N-15
Gas Centrifuge	heavier isotopes	tons	Fe, Ni, Zn, Cd, Ge, Se, Te, W, and U
Thermal Diffusion	light, stable isotopes; rare gas isotopes	tons	O-18, S-34, S-36 Ar, Ne, Kr, Xe
Distillation	light, stable isotopes		He, Li, B, and C
Chemical Exchange	light, stable isotopes	tons	C-13, N-15
Plasma separation	versatile/R&D needed	high-throughput	Indium, Ar-39
Laser separation	versatile/stable isotopes	gram/kilogram	Yb, Lu
Novel technologies	versatile	gram/kilograms	Si, Ge-76, Se-82, Mo-100, Cd-116, Te-130, Xe-136, Nd-150 MAGIS: Li-6/Li-7

Table 11. is non-exhaustive, only the most representative isotopes for each technique are cited. Apart from the current separation techniques, the same technologies can be also used to produce certain elements on a commercial level. Large quantity production of isotopes is often done via nuclear reactors or accelerators which complements the current separation technologies.

The global trends in the development of robust separation technology show the need for high purity isotopes that meet or even exceed market demands. Separation of isotopes often requires multiple stages where the output of a single-stage feeds the input of a subsequent one to meet the commercial quantities (i.e., *cascade process*). Moreover, scaling up commercially relevant quantities and the invention of machines applicable to multiple elements (versatile technology) with optimized/maximized ratio of enriched material/feedstock are also in high demand. The hybrid technologies aiming to increase the initial purity of the material before the separation takes place also recently attracted the general interest of the community (i.e., GCIS/EMIS combination). Novel separation methods (e.g., plasma ion cyclotron resonance, acoustic separation, cryogenic distillation, laser ionization, plasma centrifuge) under development promise access to less expensive, well-separated/highly-enriched elements. Apart from that, they could also lead to breakthroughs in science and new technologies.

3.3. Global Isotope Market

A large number of isotopes and almost infinite options of current, developing, and prospective applications make the global market studies the most challenging part of the report. Up-to-date, the well-established markets include segmentation into stable and unstable/radio-active elements with either large or small volume production. In addition to that, the method used to obtain an isotopic element not only determines the final characteristic (e.g., isotope purity), and the end-user applications but also the certain market category per isotope making the market studies more complex.

The traditional approach to analyze the global market led to many reports with the two most popular standing out: the Global Stable Isotopes Market and the Global Stable Isotope Labeled Compound Market. However, the deeper analysis showed that many isotopic elements that fall into both categories are produced via other techniques than EMIS due to large-scale volume market needs. Another difficulty also arises from the fact, that isotopes can be produced/separated via more than one complimentary method or simply by using the combination of the two techniques to increase, for example, the final product purity (i.e., GCIS + EMIS). The end-user application of certain isotopic element requires to analyze the global market for each isotope separately which further increase the problem complexity. In this part, the most general information regarding the global market are presented while keeping in mind that further studies are needed to establish market segment for isotopes separated via EMIS in GANIL depending on whether the valorization solution proposed is successful or not.

3.3.1. *Stable Isotopes Market*

The isotopes falling into the stable market category includes Deuterium (^{2}H), Carbon-13 (^{13}C), Oxygen-18 (^{18}O), Nitrogen-15 (^{15}N), and other stable elements. In 2018, the market size was valued to be 320 mln USD with a predicted Compound Annual Growth Rate (CAGR) of 3.0% leading to the market size of 400 mln USD in 2025 (Table 12).

Table 12. Global Stable Isotopes Market

Year	2018	2025	CAGR* (2019 – 2025)
Market size (USD)	320 mln	400 mln	3.0%

**CAGR = Compound Annual Growth Rate*

The main applications of these light elements are in the area of Nuclear Magnetic Resonance (NMR) with deuterated solvents, quantitative proteomics, metabolic research, and Magnetic Resonance (MR) for imaging/spectroscopy purposes. Another source of market data shows that the main general applications of stable isotopes are in medicine, energy, basic research, and national security.

As of February 2019, the consumer market was led by North America (49%) followed by Europe (32%) and Asia-Pacific (14%) with the U.S. being the largest consumption country with a total isotopes volume of 1160.7 kgs (in 2017). Nevertheless, the reports showed that even if the U.S. produces a significant number of isotopes, their business still relies on the foreign supplies of many elements (mostly from Russia). The U.S. Department of Energy (DOE), which is responsible for the Isotope Program (IP), often switches its policy from domestic production to buying from foreign distributors (e.g., Russia, China) depending on the national stock situation. The main problem with this kind of approach is that the U.S. isotope market relies on one foreign supply so in the case of the shortage of production there is a lack of supply security.

As far as the general stable isotope market is concerned, these elements fall into the group of isotopes belonging to the large-volume market which are produced exclusively by fractional distillation and/or chemical exchange. In this type of quantity-based market segmentation the key players are Russia (ROSATOM, 85%) and URENCO (Europe, 15%) with the production capacity of thousands of kgs/tons mostly obtained using the gaseous centrifuge separation. Main isotopes produced by these two key players are presented in Table 13.

Table 13. Large, Bulk Quantity Global Isotopes Market (main isotopes)

Market player	Key Isotopes*
ROSATOM, Russia	^{203}Tl, ^{191}Ir, ^{88}Sr, ^{68}Zn, Zn (depleted in Zn-64), ^{74}Se, ^{76}Ge, ^{28}Si
URENCO, Europe	C, Ti, Cr, Ni, Zn (leading supplier), Si, Mo, Cd, Ge, Se, Kr, W, Ir, Te, Xe

In terms of the small quantity global isotope market (production in kgs/year) supplied mostly via electromagnetic separation technology, the total market size remains unknown. However, the DOE/US report indicates that the market is primarily dominated by ROSATOM (70%) and URENCO (30%). The samples of isotopes belonging to this group are ^{50}Ti, ^{58}Fe, and ^{64}Ni needed in small quantities for NMR/Raman Spectroscopy - RS/Isotope Ratios - IRs studies. Lastly, the general global market for unstable elements is not any further analyzed assuming that the market studies have to be done for each radio-active element separately. The methods to produce these elements is also more likely to be different from EMIS (e.g., cyclotron production, nuclear reactors) making the market share negligible.

3.3.2. *Isotopes Pricing Policy*

The Department of Energy (DOE) in the USA launched in 2008-2009 a special program for the timeframe of 2009 – 2025 dedicated to production/distribution and R&D of isotopes. Following that, multiple reports related to DOE/IP published allow to access the general pricing policy and the revenue data. The final sale price divides isotopes into two groups following the simple pricing policy:

- Commercial isotopes: full-cost production recovery
- Research isotopes: subsidized price

The isotope program is fully funded by the U.S. Congress as a part of the annual budget assigned to the DOE/Nuclear Physics initiatives. The federal appropriation is dedicated to both the R&D and the Mission Readiness, facilitating generation of the products which can be further sold on the commercial market with full-cost production recovery. The funds recovered from the isotope sales are further used for both the production and the services related to such activities (cf. Figure 10).

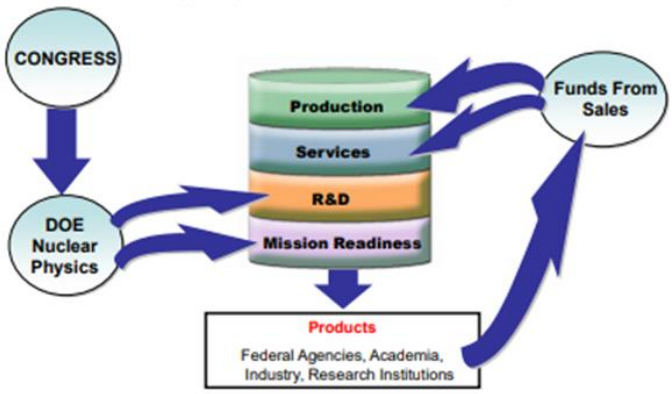

Figure 10. The U.S. Isotope Program Resources.

Since starting the Isotope Program (IP), the revenue from isotope sales nearly doubled over the first five years: from less than \$19M in 2008 up to \$37.9M in 2013 (cf. Table 14). As a consequence, the DOE/Nuclear Physics demand for the federal appropriation increased from \$18.5M in 2013 up to \$21.66M in 2016, which accelerated the isotope activities in the USA. Even though the program is still relatively small (total budget = \$56M/year in 2013), the increase in revenue and higher demand for the federal funding advocates that the isotope market is continuously growing with an increasing demand for the national production/distribution/R&D of isotopes and sale services.

The 2/3 of sale revenue in the U.S. comes from selling the Strontium-82 (^{82}Sr, radioactive) element produced via nuclear reactors, whereas, in 2011 the top-selling isotope was Nickel-63 (^{63}Ni) produced via neutron irradiation of Nickel-62 (^{62}Ni) target coming from the GCIS production. However, none of these elements is produced/separated via EMIS technology (probably due to its large market volume and/or final application).

Table 14. Isotope Program in the U.S. - Annual Financial Situation

Annual Budget	FY08	FY13	FY15	FY16
Federal appropriation	no data	$18.5M	$19.85M	$21.66M (requested)
Isotope sales	< $19M	$37.9M	$37.6M	no data
Total	**no data**	**$56.4M**	**$57.45M**	**no data**

In 2016, the recommended annual budget was $21M/year which included $4M/year for high-priority R&D (~15% of the total program), $2M/year for stable isotope separation with EMIS, $14M/year to address infrastructure investments and $1M/year for university production facility improvements. The main EMIS facility in the USA is located at Oak Ridge National Laboratory (ORNL) where DOE intends to establish a national separator for routine use for high-purity stable and long-lived isotopes separation. In 2015, the ORNL completed an effective, full intensity operation of the EMIS facility meeting the initial IP goal regarding the reduction of the U.S. dependency on foreign isotope supply.

3.3.3. *Price of Isotopes - Examples*

The commercial prices of many isotopes remain only available '*on-request*' (e.g., www.buyisotopes.com or https://www.isotopes.gov/catalog) depending on the type of element (stable/radioactive), production process, and its final quality (i.e., enrichment level/purity). Mass production via GCIS technology supplies the market with kgs/tons of the final material for a lower price. The small volume market (milligrams/grams) is dominated by the EMIS technology, which is universal but difficult to employ and expensive to run, which results in production monopoles/high price.

For example, Calcium-48 (^{48}Ca) is separated via a massive magnetic separating machine. The total market volume is 10 grams with a final price of $250 000 per one gram. The value of ^{48}Ca is high because it is a rare element with an unusual stability due to so-called 'double-magic' nucleus (i.e., 20 protons and 28 neutrons). Moreover, the ^{48}Ca is produced uniquely in Dubna/Russia via heating up the natural calcium followed by isotopic separation under high vacuum. Table 15 gives other examples of elements with their price, market size, and primary production method to illustrate the difference discussed before. Moreover, some of these prices come from the internal/external interviews due to '*on-request*' isotope pricing policy.

Table 15. Price of Isotopes with their Market Size and Production Method – examples
(grey – stable elements, blue – radioactive)

Element/Purity	Price/Market size	Production Method	Application
Lithium-6 (95%)	123 USD/gram (20 kgs/year)	Reprocessing material in the dismantlement of nuclear weapons	for nuclear weapons, targets for tritium production and fusion reactors but is also used in advanced battery research
Lithium-7 (97% or 99%)	on-request (4 kgs/year)	EMIS	for research and for pH balance in boiling and pressurized water nuclear reactors
Calcium-48 (>98%)	250 000 USD/gram (10 grams/year)	EMIS	for nuclear physics experiments (synthesis of super heavy element, studies of double beta-decay), for tracing element migration in soil and plants

Rhodium-103 (99.99%)	1 100 USD/gram (20 tonnes/year)	Reactor production (nuclear fission product of U-235)	for hardening and improving the corrosion resistance of platinum and palladium
Paladium-102 (78.18%)	1 000 000 USD/gram (100 grams/year)	EMIS	target material for Pd-103 production used in life science for healthcare and medical applications/pharmaceuticals industries); for Rh-103 production used for studies of Rh-based catalysts; for chemical yield evaluation in neutron activation analysis
Lutetium-176 (64,30 - 88,40%)	250 USD/gram (100 grams/year)	EMIS	target material for cyclotron production of Lu-177 for prostate cancer treatment with ultra-high purity
Lead-212 (various)	1 100 000 USD/gram (new market)	Reactor production (neutron irradiation of Ra-226 followed by the extracted Th-228 radioactive decay)	α-emitter for "Targeted Alpha Therapy" (TAT) for melanoma, breast, and ovarian cancer treatment
Lutetium-177 (various)	1 200 – 8 000 USD/ patient/dose (new market)	Reactor production (neutron irradiation of the Lu-176 or Yb-176 target)	β-emitter for "Targeted Alpha Therapy" (TAT) of human disease, various clinical applications

In conclusion, the final price per isotope that could be selected for a development at GANIL laboratory has to be analyzed separately for each element taking into account GANIL's cost, final product purity and the end-user application/market.

3.3.4. Isotopes in High Global Demand

The analysis of global needs for isotopes involved direct and indirect method. In the direct approach, multiple interviews were conducted with local companies present on the isotope market (stable elements) and with people working with isotopes from multidisciplinary laboratories at CEA/CNRS. The indirect method focused on analysis of most recent reports from the Nuclear Physics European Collaboration Committee (NuPECC, Long Range Plan 2017), the DOE/U.S. Isotope Program, and the Russian Federal Atomic Energy Agency (ROSATOM). The reports gives good overview of the current situation and future needs of the global isotope market.

Nuclear Physics European Collaboration Committee (NuPECC)

To start with, the isotopes list of the NuPECC report focuses on the social benefits of elements used in health, energy, environment, space, security, and cross-disciplinary applications. Following this classification the isotopes considered to be in current/future high demand are the following:

1. **Health applications:**
   - ^{3}He, ^{18}O for particle therapy
   - Lanthanum Bromide (LaBr3:Ce) for diagnostic Imaging
   - ^{48g}Sc/^{47}Sc; ^{68}Ga/^{67}Ga; ^{72}As/^{77}As; ^{83}Sr/^{89}Sr; ^{86}Y/^{90}Y; ^{110g}In/^{111}In; ^{124}I/^{131}I; ^{152}Tb/^{161}Tb; ^{152}Tb/^{149}Tb; ^{177}Lu for *'Theranostics'.*
2. **Energy applications:** next-generation fusion reactors new data models and materials able to sustain harsh conditions or liquid heavy metal coolant pool (ITER).
   - I, Te, Ru, Cs, actinide (U, Am)O_2 as fission products
   - Be, Fe, V, Cr, Mo, Nb, Ta, Zr, W for high-flux neutron test damage
   - Production of electricity in space missions (i.e. photovoltaic technology replacement)
   - ^{241}Am for nuclear power sources for deep space missions as a replacement of ^{238}Pu

3. **Security applications:** high-sensitivity portable radiation detectors.
    - ^{3}He and its alternatives ($LaBr_3Ce$, $LaCl_3Ce$, $CeBr_3$, SrI_2, Cs_2Li, $LaBr_6Ce$, Cs_2Li, YCl_6Ce) for neutron detection.
4. **Environment and Space applications:**
    - V, Ni, Cu, Zn, Pb as anthropogenic markers
    - Na, Cl, Si, Al, Ca, Fe, Ti, Sr as natural sources
    - ^{45}Ca, ^{14}C as radiotracers, for carbon dating and Accelerated Mass Spectrometry (AMS)
    - ^{10}Be for AMS
    - $^{134,135,137}Cs$, ^{237}Np, ^{241}Am, ^{3}H, ^{7}Be, ^{14}C, ^{226}Tl, ^{210}Pb, ^{214}Bi, ^{222}Rn, $^{223,226,228}Ra$, $^{228,234,235}Ac$, ^{238}U, ^{40}K, Rn, Ra are present in nuclear waste.

As the list of both stable and unstable elements is quite long, the selection of isotopes for the future EMIS method is based on whether the element has been previously separated via EMIS or not. Following that, the potential candidates for separation (and potential production) in GANIL are: Ca, K, Ru, Tl, Ta, Sr, Lu, Tb, W, Pd, Ga, and In.

Isotope Development and Production for Research and Applications (IDPRA)

The IDPRA program is the U.S. initiative in the framework of 2009 – 2025 dedicated to meet the global need for isotopes including robust infrastructures for the production of stable and long-lived isotopes. Following the shutdown of calutron in 1998 due to very high maintenance/operation cost the concern raised regarding the isotope stockpile supply in the U.S. available for no longer than 20 years. The EM method developed in the 1940s during the Manhattan Project (WWII) for uranium and then for separation of each isotope in the periodic table pushed the DOE to seek alternative solutions. As a consequence, the coordinated national IDPRA initiative started in 2009 in order to replace the calutron technology as well as to:

- **i.** Achieve purity that meets or exceeds market enquiry
- **ii.** Scale an apparatus to the production of commercially relevant quantities
- **iii.** Development of machines applicable to multiple type of elements, enriched material, and feedstock.

The first workshop of the DOE/IDPRA program took place in 2008 where 200 isotopes were discussed including identification of key elements being in short U.S. supply with no established domestic production. The IDPRA program involved 3 working groups:

1. Stable and Enriched Isotopes (e.g., **^{3}He, ^{18}O, ^{48}Ca, ^{50}Ti, ^{58}Fe, ^{64}Ni, ^{76}Ge**)
2. Radioisotopes for Research and Development (e.g., **^{18}F, ^{89}Sr, ^{90}Y, ^{131}I, ^{153}Sm, ^{211}At, ^{212}Bi, ^{224}Ra, ^{225}Ac, ^{60}Co, ^{137}Cs, ^{33}P, ^{147}Pm, and ^{210}Po**)
3. Radioisotopes and Applications (e.g., **^{99}Mo, ^{68}Ge, ^{82}Sr, ^{252}Cf, ^{241}Am, ^{63}Ni, ^{3}He, ^{60}Co, and ^{192}Ir**).

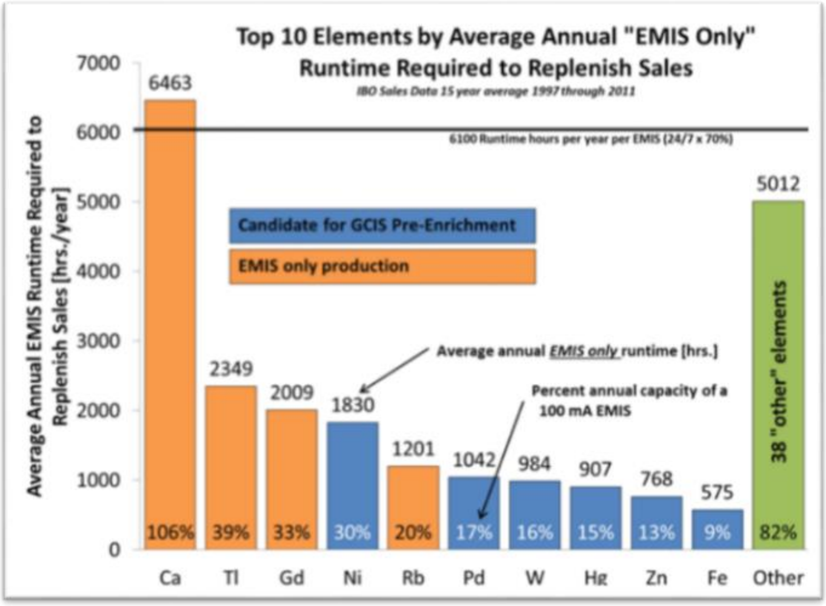

Figure 11. Top Isotopes for EMIS Production.

The EMIS prototype constructed in ORNL will meet the annual market demand for **Ca, Tl, Gd, Ni, Rb, Pd, W, Hg, Zn,** and **Fe** including the pre-enriched elements by operating 70% of the total annual time (assuming daily runtime = 24 hours) as shown in Figure 11.

Lastly, the DOE faced two significant problems regarding the U.S. isotope situation: lack of domestic EMIS production and purity concerns. As the U.S. suppliers obey the ISO 9001:2015 certified quality system, many isotopes coming from foreign sources may not possess such a formal approval. In addition to that, the lack of home EMIS separation/production results in higher costs of isotopic elements (e.g., transportation cost).

The Russian Federal Atomic Energy Agency (ROSATOM)

Last but not least, the production of stable isotopes managed by the ROSATOM Group and the Kurchatov Institute in Russia takes **~40% of the total the world's market**. Isotope production is operated in 5 production sites located in Siberia/Ural Mountains. The catalog of "available" stable isotopes is exceptionally broad and Russia remains the first step in any search for "difficult-to-source" isotopes. However, their infrastructure is heavily dependent on older EM technology (i.e., calutrons) which causes some insecurity related to future isotope production capacity. In terms of future isotope needs, the ROSATOM Development Plans were published in 2018 including the production of stable isotopes needed for nuclear medicine (**$^{142-150}$Nd, $^{162-170}$Er, $^{152-160}$Gd, and $^{168-176}$Yb**) using upgraded and expanded gas centrifuge isotope separation technology. Russia remains the main source of stable/unstable elements for domestic and international distribution including:

1. **Stable isotopes:**
    - ^{7}Li for pressurized water reactors
    - **^{48}Ca** for nuclear physics
    - ^{76}Ge and ^{28}Si for solid-state quantum memory
    - **^{74}Se** precursor to ^{75}Se used in gamma radiography
    - **^{203}Tl, ^{191}Ir, ^{88}Sr,** and **^{68}Zn** as medical radioisotope precursors
    - ^{161}Dy for Mossbauer spectroscopy.
2. **Radio-active isotopes:**
    - ^{147}Pm and ^{210}Po as micro-power source
    - ^{57}Co, ^{119m}Sn, and ^{67}Ni for Mossbauer spectroscopy.

The list of crucial isotopes produced only in Russian's calutrons is long and includes isotopes of Ca, Cd, Gd, Eu, Hg, Pd, Sm, Tl, Yb, and Zn whereas production via old EMIS technology focuses on **^{48}Ca, ^{74}Se, ^{203}Tl, ^{191}Ir, ^{88}Sr, ^{68}Zn** but also more generally **Gd, Hg,** and **Pd**, which are considered as elements in high global demand.

Isotope Production, Distribution, and R&D World-wide

Europe

In the EU there is no active commercial isotope production/separation via EMIS technology but a broad range of expertise on the R&D level exists. The Isotope mass Separator On-Line (ISOLDE) in CERN/Switzerland is the main radioactive isotope separation facility in the EU with more than 40s of experience with radioactive isotopes. Apart from that, many other universities specialize in the EMIS separation on the small-scale R&D level, such as:

- France/CSNM/Orsay
- Belgium/KULeuven
- Germany/GSI/Darmstadt
- Finland/IGISOL/Jyväskylä
- Spain/SARA/CNA/Seville
- Austria/Vienna and many others.

Nevertheless, no commercial separation/production activity via EMIS technology is observed apart from some distributors which import the separated elements from abroad (e.g., www.buyisotopes.com). Companies like URENCO present on the EU market provide certain isotopic elements obtained via other techniques than EMIS (i.e., GCIS). The EU expertise on EMIS technology can be combined in the future to build an EU-initiative to reduce foreign dependency and start a more harmonized network of producers /distributors between public and private entities. The previous isotope-related initiative include ISONET (created in 2005) with 16 partner institutions collaborating to develop the first large-scale network of stable isotopes (i.e., C, O, and H) which does not involve the EMIS technology.

USA

The USA has created the Isotope Program (IDPRA) in 2009 for the framework of 2016 - 2025 to manage both stable and unstable elements in short supply or high local/global demand. The network connects public and private entities under the supervision of the Department of Energy (DOE) resulting in structured and synchronized access to the national isotope system (cf. Figure 11). Since 2009 the Isotope Program in the USA has made dramatic improvements in operations in response to the recommendations of the initial 2009 Long Range Plan.

Figure 11. The U.S. Active Production and R&D site in 2015

The aim of the USA isotope program is to reduce foreign dependence (e.g., from Russia) and to establish national source of elements with strategic importance and high demand due to their short supply. These elements include:

- Stable: ^{3}He, ^{28}Si, ^{48}Ca, ^{64}Ni, ^{68}Zn, ^{76}Ge, ^{86}Sr (critical isotope), ^{87}Rb, ^{88}Sr, ^{96}Ru, ^{98}Mo, ^{176}Y, ^{112}Cd, ^{176}Lu, and ^{186}W.
- Radioactive: ^{68}Ge (critical isotope), ^{99}Mo, ^{137}Cs, ^{177}Lu (critical isotope), ^{211}At, ^{225}At, ^{241}Am, ^{252}Cf.

Among all these elements, the EMIS production/separation is used for ^{48}Ca, ^{64}Ni, ^{68}Zn, ^{87}Rb, ^{86}Sr, ^{88}Sr, ^{96}Ru, ^{98}Mo, ^{176}Y, ^{112}Cd, ^{176}Lu, and ^{186}W.

Russia

A similar situation is also observed in Russia where the responsibility for isotope production, distribution, and R&D is taken by the ROSATOM organization. The ROSATOM has created its own fully independent network similar to the US-DOE program. Now the actions focus on nuclear medicine and R&D centers to address the shortage in medical isotopes. The ROSATOM is currently building a new R&D center for medical radioisotopes in Malaysia.

Japan

Furthermore, the Japan Radioisotope Association (JRIA) also created an integrated system, from the supply of radioisotope products through to the management of wastes, in order to ensure the safe use of radioisotopes in Japan.

3.3.5. SUMMARY

Taking into account all three sources of information (i.e., NuPECC, DOE, and ROSATOM), the list of isotopes in high demand seems endless. Nevertheless, the chosen isotopes potentially interesting for future separation in GANIL have to be adapted to the EMIS technique. The summary of elements currently produced via EMIS or being considered in high global demand is presented in Table 16 with common elements selected and short-listed from all the reports.

Table 16. List of Isotopic Elements in High Global Demand.

NuPECC	IDPRA	ROSATOM
Ca, K, Ru, Tl, Ta, Sr, Lu, Tb, W, Pd, Ga, In	Ca, Tl, Gd, Ni, Rb, Pd, W, Hg, Zn, Fe,Sr,Ru,Mo,Y,Cd,Lu	^{48}Ca, ^{74}Se, ^{203}Tl, ^{191}Ir, ^{88}Sr, ^{68}Zn, Gd, Hg, Pd

3.4. Electromagnetic Enrichment and Purification of Isotopes – GANIL's Potential

Up-to-date, GANIL has been using the electromagnetic separation method exclusively for the production of radioactive beams in nuclear physics. Nevertheless, the wide expertise of GANIL can bring some innovation on the R&D level with the possibility of commercial market exploration in the future. In this part, the development of the EMIS technology and most recent advancements are discussed followed by the presentation of GANIL's expertise. Isotopes selected for separation in GANIL are presented with arguments supporting the final choice and technical aspects to be considered to start an EMIS activity in GANIL. In the last part, a short overview of the current and future initiatives in GANIL related to isotopes is listed to present the R&D activities within the topic.

3.4.1. GLOBAL DEVELOPMENT OF THE EMIS TECHNOLOGY

The electromagnetic isotope separation method initially invented for uranium enrichment is still widely used for the separation of versatile stable/long-lived elements (i.e., from low to high atomic mass). In principle, during the EMIS process, material feed (e.g., solid/gas form of an isotope) is introduced into the ion source where vaporization and then ionization (i.e., knocking out an electron from the atomic orbital) takes place. In the next step, charged ions are extracted from the ion source and accelerated into high speed (i.e., high kinetic energy) via interaction with an electric field. Last but not least, these ions interact with a magnetic field (exerts force) which results in a change of their movement trajectory due to the difference in the atomic mass between the isotopes of the same element. The final isotopes are collected via element-specific ion receiver followed by chemical extraction and/or further reprocessing.

Even though the history of EMIS dates back to the 1940's, many issues have been constantly addressed by continuous technological development towards a modern and cost-effective systems. Moreover, modifications of the EMIS have to address constant changes in society to meet the global demand for separated isotopes. Main aspects of EMIS development include the following elements, as presented in Figure 17:

1. **High-current ion source** for improved vaporization/ionization efficiency (from nA/mA up to A beam current intensity)
2. **Ion optics of high-current beams** for focalization of accelerated ions and reduction of the space-charge effect (i.e., the repulsion between charged ions due to Coulomb forces)
3. **Ion receiver and Isotope chemistry** for maximization of ion collection and extraction efficiency by reduction of the material loss without compromising the final isotopic purity

Figure 17. Schematic illustration of main technical challenges within the EMIS technology.

The three main problems of EMIS technology require analysis for each isotope separately, however, some main criteria for selection of the EMIS technology are:

- High selectivity and high efficiency
- Ion source (plasma mono-charged or filament ions source is element-specific)
- Form of separated isotope (gas or solid, implantation on a target).

The present study has focused on the first system of EMIS technology, i.e. the ion source and has been analyzed for isotopes selected for a GANIL potential future activity, including GANIL's expertise and added value on the technical aspects of the ion source. The ion optics, ion receiver, and chemical aspects of isotopic elements will not be discussed at this early stage of work.

To start with, one of the first ion source technologies used hot cathode arc discharge in a longitudinal magnetic field (i.e., I-22 ion source in Russia). The ions were extracted by accelerating voltage across the magnetic field through a shot. The method was invented for separation of uranium with the UF_6 working material with the vaporization temperature of 800° C and the vapor pressure of 10^{-2} Torr. As the vaporization temperature of the UF_6 was relatively high, the working material was changed for the UCl_4 (vaporization temperature of 400° C) resulting in an 80% increase of the U^+ ion current. The increase of the ion current for the I-22 Russian filament source was 20 mA, 50 mA, and 100 mA for the operation time of 2, 8 – 10, and 48 hours, respectively. The separation of U-235 with 12 – 15% enrichment in 1945 led to the mass production of 70 micrograms/day which corresponds to roughly to 25 mg/year (when assuming the uninterrupted operation time). In 1999, the upgraded version of Russian's ion source (model I-220) with 100 mA and increased operation time of 1000 hours was presented.

Similar to Russia, the USA have also been using the filament-type ion source (so-called Freeman), common in the semiconductor industry, with an ion current of 10 mA and an operation time of 40-50 hours. In the USA the main stable isotope separation activity is carried out at ORNL where the 10 mA Freeman ion source allows to separate isotopes with mass efficiency of 5 µg/hour (e.g., mainly Ba-134 but also Sr-84, Ni-64, Zr-96). Some of the most recent upgrades of the EMIS machines reported utilization of the non-ambipolar electron driven ion source (NEDIS) with 10 mA ion current for the prototyped version constructed in 2011 with the aim to reach ~100 mA source with long life operation time in 2013.

In the EU, the Versatile Arc Discharge Ion Source (so-called VADIS) is used in CERN/Switzerland to separate versatile radioactive elements. Apart from VADIS, CERN also has the Forced Electron Beam Induced Arc Discharge (FEBIAD) source developed to produce various radioactive beams other than alkali and alkaline earth to fulfill the requirements of the CERN's users. However, in both cases the limitation of the ion current (intensity in nA) makes both type of ion sources not effective for economic separation. GANIL is equipped with the FEBIAD ion source, which in principle is similar to calutron, with the same low-intensity ion current, not suitable for any high-efficiency separation; this FEBIAS ion source is used for the radioactive beam production. Nevertheless, the low-intensity plasma ion sources are effective for the acceleration of multi-charged ions making them suitable for versatile R&D applications.

It is also worth to mention the plasma Nier-Biernas ion source invented for the Accelerated Mass Spectrometry (AMS) with the ion current up to 1 A. In the Nier-Biernas ion source, the arc and the corresponding magnetic field are perpendicular to the direction of the extracted ion beam. The extracted ion-beam intensity, limited by the separator electrostatic optics, can be practically confined to the range 0.5-3 mA (in most experiments, this intensity is around 1 mA). The constancy of the extracted current intensity, essential to the stability of the electrostatic optics adjustments, is obtained by controlling the flow of the additional support gas (usually rare gas). This type of ion source has been only used on the R&D level but appears to be interesting for the commercial separation (i.e., high-current intensity). In France/Orsay, the Nier-Biernas ion source is employed within the SIDONIE separator for the production of ion beams towards the preparation of highly enriched isotopic thin targets (a few mg/cm^2) via ion implantation.

Another type of plasma-based ion source (similar to FEBIAD) is the Electron Cyclotron Resonance Ion Source (ECRIS) with an oscillating magnetic field instead of the longitudinal one. The ECR ion source is suitable to produce both mono- and multi-charged ions, due to highly dense and magnetically confined plasma with the heating of 10^3 electrons per cm^3. Lower-frequency versions (typically 2.45 GHz frequency, often using permanent magnets to provide the required 87.5 mT resonance field) are well suited to producing beams of light ions, including high-intensity and high-duty-factor pulsed beams – one such source was developed by CEA Saclay (cf. Figure 12). The mono-charged ECR (+1) is currently used for the separation of light elements in nuclear physics experiments, whereas the multi-charged one (ECR, n+) greatly accelerates heavy elements (mostly radioactive). The recent development within the ECR technology reports ion current from 5 mA up to 100 mA and long operation time for the mass separation of 0.6 g/year (5 mA) up to 3 g/year (100 mA) for H_2 isotopes.

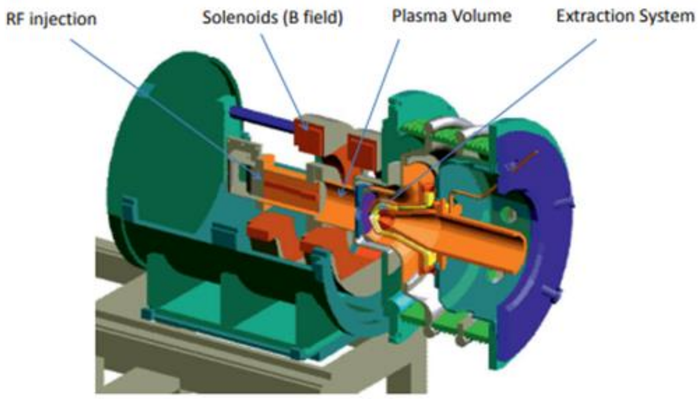

Figure 12. Layout of the SILHI 2.45 GHz ECRIS from CEA

The main advantages of the ECR ion source are modulated ion current (intensity from the nA up to A per cm^2), isotopic versatility, uninterrupted operation time, and lack of chamber contamination (in most cases), which is not the case for the filament-based ion source. The plasma ECRIS (1+) technology seems very promising for the separation of stable isotopes with continuous operation time. The Nier-Biernas ion source also appears suitable for commercial purposes, however, the maintenance service greatly limits its operation time. Comparative studies between the separation efficiency of the Nier-Biernas ion source and the ECR (+1) could be beneficial with potential for future commercial employment.

3.4.2. Most Recent EMIS Advancements

In the USA utilization of the EMIS-GCIS hybrid technology with 3 EMIS and < 50 GCIS units or 2 EMIS with < 100 GCIS units increases the output efficiency with combined ion source intensity of 300-600 mA). The most recent US activity allows for separation of 500 mg of Rh-89 for the Relativistic Heavy Ion Collider (RHIC) experiment with other stable isotopes such as Xe-129, Mo-98, Mo-100, and Yb-176. In 2015 the DOE/IP reports the development of the low-temperature ion sources as part of the Enriched Stable Isotope Production Pilot (ESIPP) with scalable, on-site isotope production. At the same time, ROSATOM in Russia works on isotopes from the platinum-palladium group with high vaporization temperature (up to 1500° C). In 2020, China reported that the Ar-39 enrichment system based on a 2.45 GHz ECRIS is under investigation, the same one as currently operating in GANIL. In Europe, there is no ongoing work related to the isotopic separation of stable elements using a versatile, low-frequency (2.45 GHz) ECR ion source apart from multiple R&D activities.

It is recommended that such a facility include several separators for a raw feedstock throughput of about 300-600 mA (10-20 mg/hour multiplied by the atomic weight and isotopic abundance of the isotope).

3.4.3. GANIL's Expertise

GANIL has a strong expertise in ECR (n+) ion sources, both for the production of stable beams (metallic ion beams in particular) and for the production of radioactive beams injected into an accelerator.

The main criteria for choosing the ECR technology for ion beam production are the following:

- High selectivity and high efficiency
- Versatile ion source (plasma mono-charged or filament ions source is element specific)
- Various forms of separated isotope (gas or solid, implantation on a target)

To start an EMIS activity at GANIL, the main competencies to be selected are:

- Electron Cyclotron Resonance Ion Source (mono-charged)
- Production of metallic beams with high energy/intensity
- Ion Optics and Mass Spectrometry expertise

Due to the wide range of corresponding competences, GANIL can bring some innovation on the R&D level. Main expertise of GANIL's include:

- Electron Cyclotron Resonance Ion Source (ECR ion source: mono-/multi-charged)
- Acceleration of ions in a cyclotron
- Production of stable metallic beams (cf. Figure 13)
- Low energy beam transport
- Mass spectrometry
- Ion optics
- Beam production/transportation with the resolution of 1/2000 or 1/3000

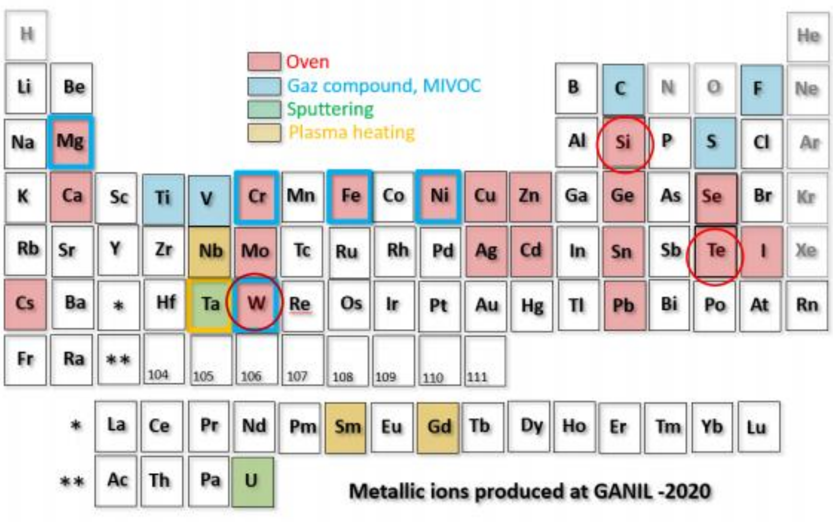

Figure 13. Metallic ions produced at GANIL (2020)

For selected elements we need to consider:

- Initial element material (oxyde, etc.)
- ECR+1 ion source injection method : oven, metal ions from the volatile compounds (MIVOC), sputtering)
- Vapor pressure

The injection method of the atomic compound inside the source chamber is a major parameter. GANIL has developed several injection methods, adapted to the various chemical metallic elements to be ionized:

- Oven (enlargement of material in crucible, good metal-vapor efficiency): Cs, Mg, Ca (70% enriched), Cr, Mo, W, Fe, Ni, Cu, Zn, Ag, Cd, Si, Ge, Sn, Pb, Te and Th (upcoming)
- Metallic Ions from Volatile Compounds – MIVOC (ion current limitation, inefficient in solid-vapor transition): Mg, Cr, W, Fe, Ni
- sputtering (low efficiency but very stable): Ta, U

An ongoing development is in progress on high-temperature ovens, for the production of high fusion temperature elements.

3.4.4. Isotopes Selected for Separation in GANIL

The WP4 Task3 aimed at studying non-medical applications of stable isotopes. Nevertheless, the global market study and the current R&D trends show that the ultra-pure stable elements are often required as target materials to produce medical-grade isotopes. To give an example, stable isotopes of Lutetium (^{175,176}Lu) are needed as target materials to produce radioactive Lutetium-177 (^{177}Lu) radioisotope for cancer therapy. An alternative method of ^{177}Lu production includes utilization of Ytterbium-176 (i.e., ^{176}Yb) instead of its concurrent ^{176}Lu. The need for ultra-pure Lutetium and Ytterbium is the key market driver to them as target materials.

Number of stable/unstable isotopes, various production/separation methods, physico-chemical properties and possible applications of isotopes makes the selection complex. Isotopes of interest extracted from the internal/external interviews led to the shorter list of popular elements (repeated more than twice) potentially interesting for the activity EMIS in GANIL (cf. Table 18).

Table 18. Summary of popular isotopes (stable/radioactive) extracted from the interviews.

Stable Elements / Main Isotope	Radioactive Elements
• Silicon: 28,29,30 / **Si-28**	• Carbon-14
• Calcium- / **Ca-48**	• Phosphorus-32,33
• Iron-52,56,57,58 / **Fe-**	• Iron-52,55
• Zinc-64,66,67,68,70 / **Zn-64**	• Zirconium-89
• Rubidium-85,87 / **Ru-87**	• Palladium-103,107
• Palladium-102,104,106,108,110 / **Pd-102**	• Xenon-133
• Gadolinium-152,154,158,160 / **Gd-157**	• Lutetium-177
• Lutetium-175,176 / **Lu-176**	• Actinium-225,227
• Yterbium-168,176 / **Yb-176**	• Lead-212
• Thallium-203,205 / **Ta-203**	• Astatine-211
• Platinum-190,192,194,196,198 / **Pt-195**	• Lead-212
• Erbium-162,164,166,167,168,170 / **Er-**	• Americium-241

When comparing this list with the various studies performed for the market identification (USA/DOE in particular), it appears that among the stable isotope list, the five most interesting that could be selected to be developed at GANIL are: calcium-48, palladium-102, ytterbium-176, lutetium-176, thallium-203.

Table 19. Fusion temperatures and Ionization energies for the 5 selected Elements

	Fusion temperature (°C) at a 10^{-4}-10^{-2}torr vapor pressure	First ionization energy (eV)
Calcium	462-600	6.11
Palladium	1200-1480	8.34
Ytterbium	360-472	6.25
Lutecium	1367-1655	5.42
Thallium	472-619	6.11

These elements have fusion temperature compatible with the high-temperature oven developed at GANIL, and rather low first ionization energies (cf. Table 19). In this range of ionization energy values, the ionization efficiency is around 1%, and some development could allow to increase it by a factor 5. Nevertheless, it will be necessary to develop high volume ovens, the existing ones being limited presently to a few hundreds of mg.

3.4.5. Projects and Initiatives Related to Isotopes in GANIL

The examples of isotope-related projects with GANIL's participation include:

- **Target Ion Source for Short-Lived Ion Production - TULIP**

The project focuses on the production of neutron-deficient medical isotopes with a relatively short half-life ($T_{1/2}$) using high intensity/high energy radioactive beam of SPIRAL2' facility. The main goals of the project include increasing the beam intensity by a factor of two, developing the Lithium beam in GANIL, and achieving sustainable production of alpha-emitting isotopes (e.g., astatine, As-211, $T_{1/2}$= 7.2 hours) using a novel approach (i.e., fusion/evaporation). The last objective can be achieved by exposing a thick target (e.g., made of carbon, for example) to high energy/high intensity (10^{12} – 10^{15} particles/s) SPIRAL2 beam. This allows producing unique elements, like As-211 for example, using a completely different method as compared to the standard one (i.e., As-211 is produced via alpha irradiation of the Thorium-222 target).

Project duration: October 2019 - September 2023 (48 months)
Project partners: GANIL and IPNO.

- **REsearch and developments for the Production of innovAtive RadioElements – REPARE**

The project focuses on the development of high-power target systems capable to sustain the high-intensity beams of the SPIRAL2 during its future operation. Apart from that, the project aims to accurately measure the production of astatine-211 (As-211), a promising radioisotope for the treatment of certain cancers. Comparison between the two production methods is envisioned. The first method includes bombarding a bismuth-209 (Bi-209) solid/liquid target with an intense helium-4 (He-4) beam. Comparison between solid and liquid targets can potentially optimize its cooling procedure as well as can help to design a more optimal production method with an online extraction of As-211. The second method is based on As-211 generation via the beta decay of radon-211 (Rn-211) in lithium induced reaction using the same Bi-209 solid/liquid target. In this approach, the $T_{1/2}$ of Rn-211 is twice longer than As-211 allowing shipping the radioactive material over an extended range.

Project duration: September 2019 - August 2023 (48 months)

Project partners: GANIL, SUBATECH, ARRONAX, LDM-TEP, and CERN.

- **PRoduction of hIgh purity iSotopes by Mass separation for medical APplication – PRISMAP**

PRISMAP initiative is more of a consortium of key European infrastructures than a research project but as long as GANIL is concerned it should be included in this part of the work. The main objective of the PRISMAP is to provide access to innovative medical isotopes with a harmonized procedure through a single internet platform. This EU initiative can be a starting point of collaboration between researchers community which are fragmented amongst university hospitals, spin-offs, SME's or large international industrial groups (e.g., academic and research groups located at universities, nuclear technology, and accelerator centers), which are already involved in a local or regional hub. The primary focus of PRISMAP are isotopes involved in radiopharmaceutical development which are used across many medical applications (e.g., theranostics, targeted therapy, and personalized medicine) notably addressing cancer. GANIL participates in the PRISMAP Work Package « Ion sources, targets, and isotope separation techniques - target design and characterization » for medical applications.

Main objectives of PRISMAP include:

- Access to new radioisotopes and new purity grades for medical research
- Creation of a common entry port and web interface to the starting research community
- Enhancing clarity and regulatory procedures to enhance research with radiopharmaceuticals
- Improvement of the delivered isotope data and regulation, along with biomedical research capacity
- Ensure the sustainability of PRISMAP in the long term.

Project duration: accepted in January 2021
Project partners: GSI, CHUV, SCIPROM, SCK-CEN, KULeuven, NPL, GANIL, ARRONAX, CERN, ILL, IST-ID, UiO, MUI, DTU, ESS, LU, TUM, NCBJ, MedAustron, INFN, JRC, PSI, CEA.

Apart from the PRIMAP, GANIL also participates in another attempt to intensify the collaboration between EU institutes which started in 2018 with the creation of the ANITA (Advanced Network for Isotope and TArget Laboratories) network. The global aim of the project is to establish a research infrastructure service for isotope and target laboratories in the EU to transfer the knowledge and improve the production techniques of well-characterized samples and targets. The target laboratories are PSI Villigen; European Commission Joint Research Centre Directorate G in Geel/Belgium; Johannes Gutenberg University Mainz & Helmholtzzentrum fur Schwerionenforschung in Darmstadt/Germany; Grand Accelerateur National d'Ions Lourds in Caen/France and University of Warsaw/Poland.

3.4.6. Local Ecosystem of GANIL

In addition to the GANIL's activities within the R&D in nuclear physics, the facility itself can benefit greatly from the local ecosystem of Caen/Normandy. The localization of GANIL allows connecting various entities in close proximity with the complementary expertise within the isotope field. The ecosystem includes both the national research laboratories and the public and/or private entities (i.e., hospitals) specializing in the following fields:

- GANIL: nuclear physics
- CIMAP: chemistry
- CYCERON: radio-chemistry
- CHU Caen: medical expertise
- ARCHADE: HADrontherapy project within the novel type of medical treatment using charged particles (e.g., protons and ions – carbon, for example).

When considering any future isotope separation/purification activity in GANIL the complementary expertise is crucial to transfer GANIL's know-how into the isotope market. The final application of isotope often requires multiple and complex procedures which have to be done in close collaboration between involved partners. This is particularly true in terms of radioactive elements when considering their half-life and potential need for transportation. The geographical localization is less important in the case of the stable elements, however, the reduction or complete elimination of short- or long-range carriage is always beneficial.

3.5. Conclusions & Recommendations

Even if GANIL is not a word-leader in terms of electromagnetic isotope separation technology, it can greatly contribute to the field by applying its 'know-how'. The following actions can be considered at GANIL in the nearest future in relation to the EMIS technology:

- GANIL can initiate collaboration / R&D project with another facility in Europe more experienced in the isotope separation field (e.g., KULeuven, OranoMed, URENCO, CERN, CEA, and CSNSM), and bring its high level expertise in the ECR ion source field. The R&D actions at GANIL could be undertaken in the following order:
    - Comparative studies of ion sources: mono-charged ECR+1 (MONO1000) with Nier-Bernas ion sources (e.g., SIDONIE/Orsay) for separation of difficult stable metallic elements (e.g., platinum, lanthanides) and those in the short list.
    - Development of versatile and efficient ECR+1 ion source for separation of stable metallic elements among the selected short list and for those which could beneficiate of a higher performance of an ECR ion source (rather than Nier-Bernas).
    - Separation of meta-stable isotopes (e.g., Lu-177m) by the mean of an electromagnetic field. Increase in mass spectrometry resolution in GANIL from 1/2000 to 1/20000 is required.
    - In a longer term future, consider a collaboration with a commercial company, if the ECR ion source efficiency is validated after the R&D action.
- GANIL can construct a R&D project with a local impact (e.g., CIMAP, CYCERON, CHU Caen etc.).
- GANIL can contribute to the building of an EU network for isotope production/distribution (similar to USA, Russia or Japan). An extension of the PRISMAP/EU project for EMIS of stable elements could also be considered.

4. Conclusion

This report presents two subjects for future potential innovation activities at GANIL. The preliminary market studies performed on these subjects, the identification of added-value from the GANIL facility and expertise, and the proposed actions allow to choose one of them (or both) to be developed in the future.