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Nuclear Data for Medical Applications Summary Report of the Technical Meeting

> IAEA Headquarters Vienna, Austria 28-31 August 2023

> > Prepared by

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February 2024

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Abstract

A summary is given of an IAEA Technical Meeting on Nuclear Data for Medical Applications at which participants assessed present and future medical applications for many radionuclides based upon their existing and potential diagnostic and therapeutic properties. Debate focused upon charged-particle induced reactions and their production cross sections, derivation of optimal yields, minimisation of radionuclidic impurities, decay-data requirements, and nuclear data requirements for proton and heavy-ion radiotherapy. Technical discussions are included in this report, along with comprehensive listings and detailed recommendations for future measurements. Subsequent excitation functions and decay-data evaluations will also be needed to ensure the necessary quality and consistency of the datasets to be assembled in an existing dedicated IAEA-NDS database that is regularly maintained and supported.

February 2024

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1. INTRODUCTION

Continued developments in medical imaging and therapy utilizing nuclear diagnostic and therapeutic techniques as well as the production of emerging radionuclides justify a further detailed review prior to further significant expansion of the existing database over an intermediate-term timescale defined as between 5 and 10 years (i.e., extended to approximately 2034). Deficiencies in specific nuclear data remain, especially with regard to obtaining the optimum production of specific radionuclides, the minimization/elimination of impurities, and the adequate quantification of various decay parameters in specific radionuclides (e.g., half-life, and α , β^+ , γ , X-ray and various electron energies and emission probabilities for comprehensive dose calculations).

All relevant nuclear data need to be critically reviewed on a regular basis, and new measurements and evaluations recommended if necessary. Therefore, a Technical Meeting on "Nuclear Data for Medical Applications" was held at IAEA Headquarters, Vienna, Austria, from 28 to 31 August 2023, in order to fulfil these requirements. A.J. Koning (Section Head, NDS) welcomed the participants, and emphasized the importance of the members' role in reassessing the nuclear data needs. The primary objective of the meeting should be to define potential future nuclear data requirements with the aims of improving preparative routes, radionuclidic purity, and the quantification of various decay characteristics to ensure confidence in consideration of patient dose. Mention was also made of a side event on more wide-ranging nuclear data needs and applications at the up-coming 67th IAEA General Conference, 25-29 September 2023. Section Head encouraged The virtual involvement/attendance at a 2-hour event entitled "Providing the best nuclear data for tomorrow's nuclear solutions: challenges and opportunities", 26 September 2023 from 14:00 to 15:30 hours, at the IAEA Conference Centre in room M7. Short invited, individual presentations will focus on nuclear reaction and structure data across the IAEA programme, as well as future "challenges, opportunities and solutions in nuclear data" based on European, US, Japanese and Chinese perspectives, with a round-table discussion on resources, competences, research infrastructures, new technology, organization and cooperation.

The IAEA-NDS organizer of the August 2023 IAEA technical meeting was R. Capote (Scientific Secretary, Nuclear Data Section). S.M. Qaim (Institut für Nuklearchemie, Forschungszentrum Jülich GmbH, Jülich, Germany) was elected Chair of the meeting, while J.W. Engle (Department of Medical Physics, University of Wisconsin, Madison, USA), A. Hermanne (Vrije Universiteit Brussel, Brussels, Belgium) and A.L. Nichols (past-time Department of Physics, University of Surrey, Guildford, UK) served as rapporteurs. The approved Agenda is attached (Appendix 1), as well as a list of participants and their affiliations (Appendix 2).

Atomic and nuclear data are required for both accelerator and reactor production of medical radionuclides, and the current status of such work organised under the auspices of the IAEA was described in an overview presented by Capote. Such nuclear data needs were initially addressed by a Coordinated Research Project (CRP) on "Charged Particle Cross-Section Database for Medical Radioisotope Production: Diagnostic Radioisotopes and Monitor Reactions" that concluded in 2001 with the publication of IAEA-TECDOC-1211 [1]. Equivalent requirements to produce therapeutic radionuclides were addressed through a further CRP on "Nuclear Data for the Production of Therapeutic Radionuclides" from 2003 to 2007.

As a result of these two initial IAEA activities, a much-needed reference online database was deployed in 2007 for the following:

⁻ monitor reactions (<u>https://nds.iaea.org/medical/medical-2020-05/monitor reactions.html</u>),

- gamma emitters (<u>https://nds.iaea.org/medical/gamma_emitters.html</u>),
- positron emitters (<u>https://nds.iaea.org/medical/positron_emitters.html</u>),
- therapeutic radionuclides (<u>https://nds.iaea.org/medical/therapeutic.html</u>).

A handbook covering reactions used for medically important therapeutic radionuclides was also published as IAEA Technical Reports Series no. 473 [2]. Earlier entries have regularly undergone a series of improvements and presentational modifications over the intervening years which are described below.

A consultants' meeting was held on "High-precision Beta-intensity Measurements and Evaluations for Specific PET Radioisotopes" in September 2008 at IAEA Headquarters, Vienna, Austria [3]. Other related consultants' meetings have been entitled "Improvements in Charged-particle Monitor Reactions and Nuclear Data for Medical Isotope Production" in June 2011 [4] (re-visit to explore possible improvements to the data of Ref. [1]), and "Intermediate-term Nuclear Data Needs for Medical Applications: Cross sections and Decay Data" in August 2011 [5]. Specific recommendations from these three consultants' meetings were brought together in 2011 to formulate and agree upon the scope, work programme and deliverables of a Coordinated Research Project on further improvements to specific charged-particle monitor reactions and nuclear data for the most efficient production and characterisation of medical radionuclides. This programme was eventually defined in terms of four published work packages that were mostly concluded in 2017/18:

- reference cross sections for charged-particle monitor reactions, *Nucl. Data Sheets* 148 (2018) 338-382; <u>https://doi.org/10.1016/j.nds.2018.02.009</u>;
- 2) recommended nuclear data for medical radioisotope production: diagnostic gamma emitters, J. Radioanal. Nucl. Chem. 319 (2019) 487–531; https://doi.org/10.1007/s10967-018-6142-4;
- recommended nuclear data for medical radioisotope production: diagnostic positron emitters, J. Radioanal. Nucl. Chem. 319 (2019) 533–666; https://doi.org/10.1007/s10967-018-6380-5;
- 4) recommended nuclear data for the production of selected therapeutic radionuclides, *Nucl. Data Sheets* **155** (2019) 56-74; <u>https://doi.org/10.1016/j.nds.2019.01.003</u>

The results were immediately included in an upgrade of the above-mentioned online databases for monitor reactions, gamma emitters, positron emitters, and therapeutic radionuclides.

As a consequence of the above and all other recent studies, another IAEA technical meeting was held in December 2018 in order to undertake a further in-depth review to assess the impact of such work and update the requirements for cross-section and decay-data measurements and various evaluations/re-evaluations of such nuclear data for medical applications [6]. Additional work was undertaken by a team of IAEA consultants starting in 2018 and still on-going, which has resulted in the following publications:

- Upgrade of IAEA recommended data of selected nuclear reactions for production of PET and SPECT isotopes, *Nucl. Data Sheets* **173** (2021) 285-308 [Ref. 7]; https://doi.org/10.1016/j.nds.2021.04.008;
- Upgrade of recommended nuclear cross-section database for production of therapeutic radionuclides, *J. Radioanal. Nucl. Chem.* 331 (2022) 1163-1206 [Ref. 8]; <u>https://doi.org/10.1007/s10967-022-08189-1;</u>
- Evaluated and recommended cross-section data for production of radionuclides with emerging interest in nuclear medicine imaging. Part 1: Positron emission tomography (PET), *Nucl. Instrum. Methods Phys. Res. B* 535 (2023) 149-192 [Ref. 9]; <u>https://doi.org/10.1016/j.nimb.2022.11.002;</u>

- 4) Evaluated and recommended cross-section data for production of radionuclides with emerging interest in nuclear medicine imaging. Part 2: Single photon emission computed tomography (SPECT), *Nucl. Instrum. Methods Phys. Res. B* **544** (2023) 165119 [Ref. 10]; https://doi.org/10.1016/j.nimb.2023.165119;
- 5) Extension of recommended cross-section database for production of therapeutic isotopes, *J. Radioanal. Nucl. Chem.* (2024), published online, January 2024; <u>https://doi.org/10.1007/s10967-023-09283-8</u>.

A recommended cross-section database for charged-particle monitor reactions is available at: https://www-nds.iaea.org/medical/monitor_reactions.html

- A recommended cross-section database for the production of gamma emitters is available at: https://www-nds.iaea.org/medical/gamma_emitters.html
- A recommended cross-section database for the production of positron emitters is available at: https://www-nds.iaea.org/medical/positron_emitters.html
- A recommended cross-section database for the production of therapeutic isotopes is available at: <u>https://www-nds.iaea.org/medical/therapeutic.html</u>

An extended database containing data from all of the above-mentioned publications and previous medical-based CRPs is also available at the IAEA medical portal:

nds.iaea.org/medportal/

2. PRESENTATION SUMMARIES

Participants' presentations are available on the IAEA-NDS web page at:

nds.iaea.org/index-meeting-crp/TM-MedApps-Aug2023/

2.1. Nuclear Data Research for the Development of Novel Medical Radionuclides, S.M. Qaim

New facilities were described that have been added to the old Institute of Nuclear Chemistry, Forschungszentrum Jülich, especially the new Cyclotron 30XP (IBA) and laboratories for radionuclide production work. A brief overview was given of new directions in radionuclide applications, e.g., developments identified with theranostics, bimodal imaging, immunoPET, radioactive nanoparticles and radionuclide targeted therapy. All of these emerging applications require novel metallic radionuclides which are more versatile than more commonly used radionuclides, organic elements, and halogens. Although a large number of novel radionuclides could be considered, the emphasis is presently on "non-standard" positron emitters. The development of production methodologies for such novel radionuclides involves studies of several important topics, i.e., nuclear data, high-current targetry, chemical processing, and quality control of the product.

This presentation was devoted to specific nuclear data requirements for the accelerator-based production of "non-standard" positron emitters. Therefore, the following important and highly-relevant topics were discussed:

- Positron emission intensities of novel positron emitters, especially the necessity of undertaking direct measurements.
- Low-energy data up to 30 MeV: while the database is in good shape and all evaluated data are available on the IAEA website, the threshold regions of a few reactions demand more attention.
- The database in the intermediate-energy range is weak, and theoretical predictions have only been partially successful. Evaluations are of no help in these circumstances, but

rather extensive experimental work and further theoretical developments are more appropriate.

- Alpha-particle beams are becoming very important. More data are needed with regard to the production of radionuclides by means of alpha particles, especially high-spin isomeric states and rare-earth radioisotopes.
- The d(Be) and d(C) break-up neutron sources are potentially very promising, especially for the production of radionuclides via (n,xp) or via (n,2n) reactions if the product decays to a medically-useful daughter nuclide.

Accelerator-based production of radionuclides is receiving great impetus worldwide, and the necessary supply of good nuclear data should be assured. Longer-term requirements will depend on future emerging medical applications.

2.2. Extension of the Recommended Cross-section Database for the Production of Therapeutic Isotopes and Charged-particle Monitor Reactions, *F.T. Tárkányi*

Work performed in collaboration with A. Hermanne, A.V. Ignatyuk, F. Ditrói, S. Takács and R. Capote Noy

New evaluated cross-section data were produced for the production of radionuclides with emerging interest for therapeutic use in nuclear medicine, identified mostly with the recommendations from the IAEA-NDS Technical Meeting on Nuclear Data for Medical Applications in Vienna, 10-13 December 2018 (see Ref. [6]). Results include 62 charged-particle induced nuclear reactions of interesting for production of the ⁴⁷Sc, ⁴⁷Ca(⁴⁷Sc), ^{58m}Co, ⁷¹As(⁷¹Ge), ⁷¹Ge, ⁷⁷Br, ^{80m}Br, ¹⁰³Pd(^{103m}Rh), ¹⁰³Ru(^{103m}Rh), ¹⁰⁵Rh, ^{117m}Sn, ¹¹⁹Sb, ¹³⁴Ce, ¹³⁵La, ¹⁶¹Tb, ¹⁶⁵Er, ¹⁶⁵Tm(¹⁶⁵Er), ¹⁶⁷Tm, ^{197m}Hg, ^{197g}Hg and ²³⁰Pa(²³⁰U).

The recommended database for charged-particle monitor reactions has also been extended to include 53 charged-particle induced reactions on C, Al, Ti, Fe, Ni, Cu, Nb and Au. These new data permit the simultaneously study of a few reactions on the same target, the use of backings for electrodeposited and sedimented targets, and extensions to higher-range beam energies.

Recommended cross sections over well-chosen energy domains have been determined, with their uncertainties and calculated physical yields based on the above studies and analyses. A technical paper that describes the work undertaken was published online in January 2024: doi.org/10.1007/s10967-023-09283-8 ("Extension of recommended cross-section database for production of therapeutic isotopes", *J. Radioanal. Nucl. Chem.* (2024)).

2.3. Cyclotron Production of Innovative Radionuclides: Nuclear Data Research Activities at INFN-LNL, G. Pupillo and L. Mou

One major aspect of the SPES (Selective Production of Exotic Species) research project is the cyclotron-based production of radionuclides for medical applications at the Legnaro National Laboratories of the National Institute for Nuclear Physics (INFN-LNL). A primary feature of SPES is the 70-MeV proton cyclotron with dual-beam extraction, which was installed in 2015 within a new building equipped with ancillary laboratories that are close to completion. The construction of an advanced ISOL (Isotope Separation OnLine) facility is also planned to produce re-accelerated exotic ion beams for nuclear physics studies. Double-beam extraction of the cyclotron allows multidisciplinary activities to be performed, such as radionuclide production for medical applications and neutron-based nuclear physics research. Results are reported from the interdisciplinary LARAMED (LAboratory of RAdionuclides for MEDicine) project on nuclear cross-section measurements, along with related plans for the next few years. We have mainly focused on ⁶⁷Cu and ⁴⁷Sc proton-induced reactions, in particular the ^{68,70}Zn(p,x)^{67,64}Cu cross sections and those for ^{nat}V, ⁴⁸Ti, ⁴⁹Ti and ⁵⁰Ti enriched targets. Attention was also paid to the homogeneity and characterization of these targets used, and

measurements of all co-produced contaminants. Work is also underway on medical Tb isotopes, specifically the ¹⁵⁵Gd(p,n)¹⁵⁵Tb and ¹⁵⁹Tb(p,5n)¹⁵⁵Dy(EC)¹⁵⁵Tb reactions. As for the future, we plan to study the ^{nat}Dy(p,x)¹⁶¹Tb, ¹⁵²Gd(p,n)¹⁵²Tb and ¹⁵²Gd(p,4n)¹⁴⁹Tb reactions. Collaborative work with Italian and French colleagues has also underlined the need for additional nuclear data involving light charged particle beams for emerging medical radionuclides, such as ⁶⁷Cu, ⁴⁷Sc, ⁸⁹Zr, ¹⁰³Pd, ^{186g}Re, ⁹⁷Ru and ²¹¹At [11].

2.4. Production Yields of ⁶⁴Cu and ⁶⁷Cu, Y. Nagai

⁶⁴Cu and ⁶⁷Cu have nuclear and chemical properties suitable for theranostic applications. However, the low availability of both ⁶⁴Cu and ⁶⁷Cu has delayed the development of radiopharmaceuticals containing these two radionuclides. We have been working on the production of ⁶⁴Cu and ⁶⁷Cu by the ⁶⁴Zn(n,p)⁶⁴Cu and ⁶⁸Zn(n,n'p+d)⁶⁷Cu reactions by means of a neutron source generated from a deuteron accelerator [12]. Fast neutrons based on this neutron source are produced by irradiating a natural carbon target with a deuteron beam. A carbon target has advantages, such as a high melting point (3550°C), excellent machinability, low cost, and easy plant maintenance due to the short half-life of the radioisotopic by-products.

Our neutron source has the following characteristics suitable for the mass production of ⁶⁴Cu and ⁶⁷Cu of high specific activity:

- Fast neutrons are emitted from the neutron source mainly in the forward direction relative to the deuteron beam direction. Therefore, most of the emitted neutrons are used to produce these radionuclides by placing enriched samples of ⁶⁴Zn and ⁶⁸Zn in the direction of the deuteron beam.
- Neutrons from the C(d,n) reaction at a deuteron energy of 40 MeV have a continuous energy spectrum from thermal to about 40 MeV, with a most probable energy of 14 MeV. At neutron energies between a few and 20 MeV, the (n,p), (n,d), (n,n'p) and (n,α) charge-exchange reaction cross sections are large for stable nuclides with masses below about 100. Consequently, carrier-free radioisotopes can be chemically separated from neutron irradiated samples with high specific activity.
- As a result of the zero charge of the neutrons, Zn samples weighing more than 100 g can be used for high-intensity neutron irradiation for the mass production of ⁶⁴Cu and ⁶⁷Cu. Therefore, a two-step separation method has been developed for the rapid separation and recovery of high quality ⁶⁴Cu and ⁶⁷Cu from large quantities of Zn samples irradiated with accelerator-based neutrons [13]. This method combines sublimation of irradiated Zn samples and column separation of the sublimation residues.

Production yields of 64 Cu and 67 Cu have been measured by irradiating three metal zinc tablets of 20 mm diameter (17.551, 18.136 and 19.714 g and total thickness of 32 mm) with neutrons produced by the Be(d,n) reaction from 40-MeV, 5- μ A deuterons provided by the AVF cyclotron at Cyclotron and Radioisotope Center (CYRIC), Tohoku University [13]. The arrangement of these three samples to allow the yields to be measured separately was intended to provide a rigorous check of the measured energy and angular distributions of the accelerator neutrons, including the evaluated cross sections.

The estimation of the ⁶⁴Cu and ⁶⁷Cu yields was performed by numerical calculations in which the data on the double-differential cross section of the neutron flux and the neutron-nucleus reaction cross sections given in the fourth version of the Japanese Evaluated Nuclear Data Library (JENDL-4.0) were adopted [14, 15]. The estimated yields of ⁶⁴Cu and ⁶⁷Cu for each set of ^{nat}Zn samples agree with the measured yields within an uncertainty limit of 20%. Total systematic uncertainties in the calculation were estimated to be 23% by considering uncertainties associated with the measured neutron data of the ⁹Be(d,n) reaction with an uncertainty of 18% and the evaluated cross sections with an uncertainty assumed to be 15%,

while total systematic uncertainties in the experimental values were calculated to be 12% by consideration of the uncertainties associated with the distance between the Be target and the sample position, etc. [13]. On the basis of these results and immediately after irradiating 50 g of enriched ⁶⁴Zn and ⁶⁸Zn samples with accelerator neutrons obtained with a 40-MeV, 100- μ A deuteron beam for 13 and 24 h, the yields of ⁶⁴Cu and ⁶⁷Cu were estimated to be 26 and 1.5 GBq, respectively.

Following on from our experimental studies of medical radioisotope production by means of a deuteron accelerator-based neutron source, we have launched the <u>D</u>euteron <u>A</u>ccelerator for <u>T</u>heranostic m<u>E</u>dicine (DATE) project at the Tohoku University Cyclotron Facility. Thus, the deuteron-beam intensity has been increased from 5 to 100 μ A for 25 to ~ 40 MeV energy by installing a negative deuterium ion source (D-) and stripper foil at the operational CYRIC facility. This project is expected to pave the way for the domestic production of short-lived medical radioisotopes.

2.5. TALYS for Charged-particle Cross Sections: Predictive Power and Parameter Fitting, A.J. Koning

New versions of TALYS and TENDL will be released at the end of 2023. A large review paper of the code has also just been published [16]. Since the first release of TALYS 20 years ago, about 6000 papers have, in one way or another, used TALYS or TENDL. A few improvements relevant to the production of medical isotopes can be listed for the next release:

- A JSON-structured database with a list of 8500 experimental cross-section data sets that have been declared outlier/inlier on the basis of fit-by-eye, using nuclear data libraries and other experimental data sets.
- A directory structured database EXFORtables represents an attempt to make the entire EXFOR computer-readable for at least the cross sections. Automatic normalization to newer monitor data sets and decay data have been applied.
- Assessment of the uncertainty ("predictive power") of TALYS when used with entirely global parameters without any prior knowledge of the experimental data of one particular nuclide,
- Optimization of a small number of TALYS input parameters (< 6) to the experimental data selected as "in-liers" by using the soon-to-be released TASMAN code.

The current predictive power of a "blind" TALYS calculation is argued to be around 30% near the peak of a (p,n) excitation function and 40% for (p,2n). This uncertainty should be taken into account if cross sections from TENDL-2021 are used for reaction channels for which no experimental data exist. The 232 Th(p,x) 225 Ac reaction is used at higher energies to illustrate the difference between a completely global prediction (giving a deviation of up to a factor of 3), and fitted TALYS results for both the required isotope and the impurities by changing one TALYS input parameter for the fission barriers.

The examples suggest TALYS can be used as a pure prediction code (where "predictive" ranges from reasonable to bad, depending on the reaction channel), but also as a fitting code where several parameters that include purely phenomenological energy-dependences of some model parameters can be used to achieve a perfect fit. Of course, the physics for that particular case is then lost.

The latter would be an alternative approach to the Padé approximation, but requires time to develop, and may be investigated in the future. An advantage over a non-model fitting approach would be that the prediction of impurities is obtained in the same calculation, while this is

constrained by a very good fit to the channels for the required isotope for which enough experimental data may be available.

2.6. Model Considerations for ⁴⁷Sc Production Data from Enriched Titanium Targets, and for ¹⁵⁵Tb Production Data from Enriched Gadolinium Targets, *L. Canton*

Work performed in collaboration with F. Barbaro, Y. Lashko, L. Zangrando, N. Uzunov, L. De Nardo and L. Melendez-Alafort

We have analysed the low-energy production cross sections of medical radionuclides ⁴⁷Sc (Beta therapy and SPECT) and ¹⁵⁵Tb (SPECT and Auger/CE emissions), based on highly-enriched titanium and gadolinium targets, respectively. Potentially, these production routes could become widespread considering the establishment of hospital cyclotrons worldwide, with their numbers also increasing rapidly increasing in developing countries.

TALYS calculations have been employed, based upon two different approaches [17]:

- We have compared the existing experimental data on enriched target with the variability
 of reaction models that can be selected with the input parameters. This model variability
 has been represented by band plots delimited by first and third quartiles, thus representing
 the model variability as an extension of the Box-Wishker plot to the continuum.
- We have introduced a novel optimization scheme based on Genetic Algorithms, that efficiently fit selected data against given parameter variations of the TALYS code. Based on sound theoretical models, the fitting procedure allows for a certain degree of extrapolation in both low-energy and high-energy regimes, something that cannot be accomplished with approaches based on polynomial or equivalent-type fitting.

With these tools, we have analysed the production routes ${}^{49}\text{Ti}(p,2pn)$, ${}^{50}\text{Ti}(p,\alpha)$ and ${}^{49}\text{Ti}(d,\alpha)$ with the following results:

- There is no energy window possible for ⁴⁹Ti(p,2pn)⁴⁷Sc production with the required purity for medical applications. This is due to the combined co-production of the contaminants ⁴⁶Sc (half-life much larger than ⁴⁷Sc) and ⁴⁸Sc (half-life just over 1/2 that of ⁴⁷Sc) which prevents high-purity production of ⁴⁷Sc.
- Thanks to the comparison with the ⁵⁰Ti(p, α) data of 2022 by the Bern-PSI group and preliminary data from the REMIX-INFN-LNL experiment with an enriched ⁵⁰Ti target, the TALYS cross sections can be optimized, and yields derived along with radionuclidic and isotopic purity. These results indicate that this production method provides ⁴⁷Sc of medical-grade purity, and is well suited for hospital cyclotron delivery (E_{max} lower than/equal to 18 MeV) with a reasonably significant yield.
- Cheng 1964 measured with an enriched target the ⁴⁹Ti(d,α)⁴⁷Sc excitation function that is fairly consistent with the TALYS calculation when considering model variability. Furthermore, co-production of ⁴⁶Sc appears somewhat lower than expected. New measurements would be very beneficial to clarify this point. However, both calculations and measurements suggest that ⁴⁷Sc production with deuterons of 10 MeV maximum energy is essentially free of contaminants (⁴⁶Sc and ⁴⁸Sc). Therefore, this production route is also suitable for ⁴⁷Sc of medical-grade purity. When fitted with the TALYS code by means of Genetic Algorithms, the Cheng data show that a significant yield is obtained which is well suited for pre-clinical studies at the very least. However, one must also bear in mind that mass production codes are not yet able to cope with the deuteron break-up component in the description of nuclear reactions with deuteron beams (codes such as TALYS, EMPIRE, etc.), so their predictions are less reliable than with protons and alpha beams.

We have also analysed the ¹⁵⁵Gd(p,n)¹⁵⁵Tb production route, measured recently by the Bern-PSI group using an enriched ¹⁵⁵Gd target [18]. TALYS modelling appears to be quite consistent with the new data, including contaminant production. Co-production of ¹⁵⁶Tb is an unfortunate feature of this approach, and can be ascribed to trace-level contamination of the enriched ¹⁵⁵Gd target with ¹⁵⁶Gd. A close interdisciplinary collaboration with medical physicists expert in dosimetry calculations and imaging analysis leads to the following conclusion: ¹⁵⁵Tb can be produced with a quality suitable for medical applications by means of low-energy proton beams (maximum of 10.5 MeV) and ¹⁵⁵Gd-enriched targets, if the content of ¹⁵⁶Gd does not exceed 2%. Under these conditions and considering the bio-kinetics of the Tb-cm09 DOTA-folate complex, the dose increase due to the presence of contaminant radioisotopes remains below the 10% limit, and good quality images comparable to those of ¹¹¹In can be guaranteed.

2.7. Input, Output and Lessons Learned: PET and SPECT Evaluations Based on IAEA Technical Meeting, Vienna, 2018, A. Hermanne

Two articles have been prepared for publication on the evaluation of experimental datasets and production of recommended cross sections with uncertainties, based on the proposed reactions for PET and SPECT radioisotopes listed in the summary report of the previous IAEA-NDS technical meeting held in Vienna, December 2018 [6]. These radionuclides and production reactions are listed in Tables 1 and 2, and are fully discussed in two separate papers [9, 10]. A total of 15 radionuclides with two parents, 53 reactions and 26 fits were included for PET, while the equivalent SPECT studies focused on 12 radionuclides with one parent, 39 reactions and 28 fits. Both articles include a detailed table of the adopted decay data of the reaction products investigated that are based on the contents of ENSDF, 2020 [19]. Summary of the methodology:

- Full survey and compilation of literature for experimental cross-section data.
 Essentially rely on data available in EXFOR for numerical values.
- Correct (if needed) published data sets for both outdated values of monitor cross sections and for nuclear decay characteristics.
- Compare published experimental datasets with theoretical calculations (online data from TENDL-2019 and TENDL-2021 libraries).
- Select acceptable data sets, and motivate de-selection.
- Fit the selected data by means of the Padé statistical approach.
- Recommended data with overall uncertainties were produced (including assumed systematic uncertainty of 4%);
- Calculate integral production yields on the basis of recommended fitted data and their uncertainties.

Some selected reactions or isotope observations of importance to future evaluations were illustrated and discussed within the presentation:

- Re-evaluations of nuclear decay data are required at regular intervals of time remarks were made by Bleuel, *et al.*, in 2021 concerning recommended but no longer valid values for the ^{nat}Ni(d,xn)⁶¹Cu monitor reaction, that arise from changes in the ratio of abundance for the 282.956- and 658.008-keV γ lines of ⁶¹Cu [20].
- Time delays between a first evaluation/fit and final acceptance of an article can result in the appearance of additional highly-relevant publications that can impact on the original data selection. As an example, in Subsection 3.9.1 of Ref. [9] for the ⁷⁵As(p,4n)⁷²Se reaction, two data sets were available at the first cut-off date in mid-2021 and an additional set was available at review 15 months later, resulting in a change of selection.

- Even for the formation of a radionuclide on natural targets whereby multiple reactions of different stable isotopes will occur, many different cross-section measurements can be in good agreement and the selection process is easy. For example, in Subsection 3.1.2 of Ref. [9] for the ^{nat}T(p,x)^{44m}Sc reaction there are five stable Ti isotopes, with 16 datasets up to 200 MeV in existence and only one data point was de-selected.
- However, for other reactions with a rather large number of available data sets, much disagreement can also occur (see Subsections 3.10.2 and 3.10.3 of Ref. [9] for the ^{nat}Br(p,x)⁷⁶Kr and ⁷⁹Br(p,4n)⁷⁶Kr reactions, there are nine reference data sets, but no satisfactory fit is possible).
- An accurate experimental determination of the cross sections for the cumulative formation of a longer-lived isotope requires a decay period of at least four half-lives of the shorter-lived parent/metastable state to be observed before measurements are made. Consider separately given cross sections for the metastable and ground states, whereby a correction factor has to be included in the weighted summation that depends on the ratio of their half-lives. A extended discussion is available in Subsection 3.2 of Ref. [9] on the formation of ^{87m}Y and ^{87g}Y(m+) on ^{87,88,nat}Sr targets.
- If a data set is systematically different from multiple sets in good agreement, the implementation of a constant normalization factor is sometimes a solution to obtaining agreement. Consider Subsection 3.10.1 of Ref. [10] dealing with the natTl(p,x)²⁰³Pb reaction in which five data sets were available: one was deselected, and one multiplied by a factor of 0.75 to be in agreement with the maximal value of another selected data set.

The main lessons learned while finishing these publications are that teamwork is needed for all steps (input, selection, analysis of fits and final publication), and that data selection is not unique nor a standard procedure.

Isotope/Reaction	Proposal in [6]	Fit	Comments
^{nat} Cl(p,x) ^{34m} Cl	proposed	Padé	
$^{35}Cl(p,pn)^{34m}Cl$	proposed	no	normalisation of ^{nat} Cl up to 30 MeV
$^{34}S(p.n)^{34m}Cl$	proposed	no	two data sets. scattered data
$^{31}P(\alpha.n)^{34m}Cl$	proposed	no	only one data set
$^{nat}S(\alpha,x)^{34m}Cl$	proposed	no	only one data set
36 Ar(d α) ^{34m} Cl	added	no	only one data set
$^{34}S(d,2n)^{34m}Cl$	proposed	no	no data found
$^{35}Cl(\alpha n)^{38}K$	proposed	Padé	
40 Ar(n 3n) ³⁸ K	proposed	no	only one data set
$^{38}Ar(p,n)^{38}K$	proposed	no	only one data set
40 Ca(α .x) 43 Sc	proposed	Padé	, i i i i i i i i i i i i i i i i i i i
${}^{40}Ca(\alpha,n){}^{43}Ti(\beta^+){}^{43}Sc$	proposed	no	combined with ⁴⁰ Ca(α .x) ⁴³ Sc
$^{43}Ca(p.n)^{43}Sc$	proposed	Padé	
$^{42}Ca(d,n)^{43}Sc$	proposed	no	only one data set
45 Sc(p,p) 45 Ti	proposed	Padé	
$^{45}Sc(d.2n)^{45}Ti$	proposed	Padé	
$54 \text{Fe}(\mathbf{p} \boldsymbol{q})^{51} \text{Mn}$	proposed	Padé	
54 Fe(d gn) 51 Mn	proposed	no	no usable data 5^{1} Cr in parallel
${}^{50}Cr(d n)^{51}Mn$	proposed	Padé	no usuble data, "Er in paraner
$^{nat}V(^{3}\text{He x})^{51}\text{Mn}$	proposed	no	only one data set
$^{\text{nat}}\text{Fe}(\mathbf{n},\mathbf{x})^{51}\text{Mn}$	proposed	no	limited high-energy data, only one data set
$natNi(p,u)^{61}Cu$	proposed	no	available online, no new data
${}^{59}Co(a 2n)^{61}Cu$	added	Padé	available online, no new data
$69 \text{Ge}(n, n)^{69} \text{Ge}(n)$	nronosad	Dodá	
$^{nat}Ga(p,n)^{69}Ga$	proposed	Padé	
Ga(p,xn) Ge	proposed	Padé	and data set 1 noint not recommanded
69Ca(d,2n) 69 Ca	proposed	raue	one data set + 1 point, not recommended
$hat Zn(\alpha, xn)^{69}Ga$	proposed	110 Dodá	no specific data available
$\sum \prod(u, x \prod) Ge$	added	Padé	
$^{75}\Lambda_{\rm s}(p,y)^{69}$ Ca	added	Pade	only one data set
⁷² G (,) ⁷² A	added		only one data set
$72Ge(p,n)^{72}As$	added	Pade	1 1
$^{72}\text{Ge}(d,2n)^{72}\text{As}$	added	no	only one data set
75 As(p,4n) 72 Se(EC) 72 As	proposed	Pade	
75 As(d,5n) 72 Se(EC) 72 As	proposed	Padé	
$^{70}\text{Ge}(\alpha,2n)^{72}\text{Se}(\text{EC})^{72}\text{As}$	added	Pade	
$ratBr(p,x)^{72}Se(EC)^{72}As$	added	no	only one data set
$\frac{1}{2} \frac{B}{2} \frac{B}$	added	no	only three points, all at high energy
$^{\prime 0}$ Se(p,n) $^{\prime 0}$ Br	added	Padé	
100 Br 79 Dr $(-4\pi)^{76}$ Kr $(EC)^{76}$ Br	proposed	no	possible parent, data disagree
⁷ Br(p,4n) ⁷⁰ Kr(EC) ⁷⁰ Br	proposed	no	possible parent, data disagree
$^{\text{nat}}\text{Rb}(p,xn)^{63}\text{Sr}$	proposed	Padé	
⁶³ Rb (p,3n) ⁶³ Sr	proposed	Pade	
$^{\text{nar}}\text{Kb}(d,xn)^{83}\text{Sr}$	added	no	only one data set
$\operatorname{Mat}_{Kr}(\alpha, xn)^{65} Sr$	added	no	only one data set
⁸² Kr(31L 20) ⁸³ Sr	added	no	only one data set
83 Kr(3 He,2n) 83 Sr	added	no	only one data set
$\frac{1}{89} \frac{1}{100} \frac{1}{$		IIO Dadź	omy one data set
ratc 1(p,4n) $ratc 1(p,4n)$ $ratc 1(p,4n)$	proposed	Pade	
$155 \text{ C} = 4 \text{ (p,xn)}^{152} \text{ I} \text{ b}$	added	Pade	
h^{100} Gd(p,4n) ¹⁰² 1 b nat Cd(d,, h^{152} Th	proposed		
$152 \text{ C} \text{ d} (\text{d}, \text{XR})^{3/2} \text{ I} \text{ D}$	added		
159 TP ($a_{1} > 152$ TP	auded	Pade	
$100 10(p,x)^{102} 10$	added	no	two data sets, no overlap

TABLE 1: Potential radionuclides proposed and considered for PET (2022/2023).See available data at: https://www-nds.iaea.org/medical/positron emitters.html

TABLE 2: Radionuclides proposed and considered as non-standard $\beta^{\scriptscriptstyle +}$ emitters and for SPECT (2022/2023). See available data at: <u>https://www-nds.iaea.org/medical/gamma_emitters.html</u>

Isotope/Reaction	Proposal in [6]	Fit	Comments
^{nat} Ti(p,x) ^{44m} Sc	added	Padé	yield limited to 70 MeV in figure
^{nat} Ti(d,x) ^{44m} Sc	added	Padé	
⁸⁷ Sr(p,n) ^{87m} Y	added	Padé	
⁸⁸ Sr(p,2n) ^{87m} Y	added	Padé	
$^{nat}Sr(p,xn)^{87m}Y$	added	Padé	
${}^{87}{ m Sr}(p,n){}^{87g}{ m Y}(m+)$	added	Padé	
88 Sr(p,2n) 87g Y(m+)	added	Padé	
$^{nat}Sr(p,xn)^{8/g}Y(m+)$	added	Padé	
$^{nat}Sr(d,xn)^{8/m}Y$	added	no	only one data set
$^{nat}Sr(d,xn)^{8/g}Y(m+)$	added	no	only one data set
$^{85}\text{Rb}(\alpha,2n)^{8/\text{m}}\text{Y}$	added	Padé	
85 Rb(α ,2n) 87g Y(m+)	added	Padé	
$^{nat}Sr(p,x)^{88}Y$	added	Padé	
$^{nat}Sr(d,x)^{88}Y$	added	no	only one data set
¹⁰³ Rh(p,x) ⁹⁷ Ru	proposed	Padé	
⁹⁹ Tc(p,3n) ⁹⁷ Ru	proposed	no	only one data set
$^{nat}Mo(\alpha,xn)^{97}Ru$	proposed	Padé	
^{nat} Ru(p,xn) ⁹⁷ Ru(cum)	added	no	two data sets, not enough overlap
^{nat} Ru(d,xn) ⁹⁷ Ru(cum)	added	no	two data sets, not enough overlap
130 Te(d,x) 131 I(cum)	added	Padé	
$^{nat}Gd(d,x)^{159}Gd$	added	Padé	
^{nat} Gd(p,xn) ¹⁵⁵ Tb	added	no	not enough overlap
¹⁵⁵ Gd(p,n) ¹⁵⁵ Tb	proposed	Padé	
156 Gd(p,2n) 155 Tb	proposed	Padé	
¹⁵⁵ Gd(d,2n) ¹⁵⁵ Tb	proposed	no	no data
$^{nat}Gd(d,xn)^{155}Tb$	added	Padé	
$^{nat}Er(p,xn)^{167}Tm$	added	Padé	
167 Er(p,n) 167 Tm	added	Padé	
$^{nat}Er(d,xn)^{167}Tm$	added	Padé	
^{nat} Yb(p,x) ¹⁶⁷ Tm	added	no	only one data set
$^{nat}Yb(d,x)^{167}Tm$	added	Padé	
165 Ho(α ,2n) 167 Tm	added	Padé	
169 Tm(d,x) 167 Tm	added	Padé	
¹⁶⁹ Tm(p,3n) ¹⁶⁷ Yb(EC) ¹⁶⁷ Tm	added	Padé	short-lived parent
$^{nat}Os(d,x)^{191}Os$	proposed	no	two data sets, not enough overlap
$^{nat}Os(p,x)^{191}Os$	added	no	only one data set
^{nat} Tl(p,xn) ²⁰³ Pb	added	Padé	
$^{nat}Tl(d,xn)^{203}Pb$	added	Padé	

2.8. Nuclear Data Needs for Medical Radionuclide Producers, J.W. Engle

The Cyclotron Research Group at the University of Wisconsin actively pursues the production and application of many radionuclides in partnership with a local and nationally distributed user base and is a member of the US DOE University Isotope Network. Several nuclear decay and reaction data measurements have also been published by the group that are highly relevant to these radionuclides.

Several nuclear data requirements have become apparent since the previous IAEA TM on the topic in 2018:

- As a consequence of the recent, rapid growth in clinical applications of medical radionuclides, there has been an intensifying need for evaluations of the radionuclidic impurities that are co-produced along with the desired radioactive products of very welldescribed nuclear reactions. Measured data exists for many of the impurity-producing reactions.
- There is a need for highly accurate data near nuclear reaction thresholds, especially for low-energy reactions relevant to commercial cyclotrons that produce the bulk of the world's supply. Example cases discussed include ⁸⁹Zr production from ^{nat}Y targets that avoid ⁸⁸Zr, and ⁶⁸Ga from ⁶⁸Zn that avoid ⁶⁷Ga and ⁶⁶Ga.

Additional reaction needs include measurements of the formation excitation functions of Auger-emitting radionuclides, especially ^{117/119}Sb, ⁷¹Ge, and the mass-103 isobar.

2.9. A New Set of Cross Sections to Produce β⁺ Emitters (¹¹C, ¹²N, ¹³N, ¹⁵O, ²⁹P and ^{38m}K), C. Guerrero Sanchez

Work performed in collaboration with T. Rodríguez-González and J.M. Quesada

Thanks to superior depth-dose distribution when compared with conventional photon therapy, proton therapy allows the maximization of the deposited dose inside the tumour while reducing the dose in healthy tissues. However, uncertainties in the beam range require further consideration of additional safety margins to ensure tumour coverage and the non-irradiation of surrounding tissues. A method to validate the range of the beam *in-vivo* should lead to better treatment designs, minimizing normal tissue complications and hence improving tumour control. Among the different options, PET range verification has received significant attention, and has even been clinically tested.

PET range verification requires a comparison of the measured (PET scanner) and expected (Monte-Carlo simulations) β^+ activity distributions produced by the proton field in the patient's body, which can be online (ms to s) or off-line (minutes) depending on the half-life of the radioisotope involved. The accuracy of the expected activity distribution is dominated by the production cross sections of the β^+ emitters of interest: ¹¹C (t_{1/2} = 20.36 min.), ¹³N (t_{1/2} = 9.97 min.), and ¹⁵O (t_{1/2} = 122 s), produced in C, N and O, ¹²N (t_{1/2} = 11.0 ms) produced in C, ²⁹P (t_{1/2} = 4.14 s) produced in P, and ^{38m}K (t_{1/2} = 926 ms) produced in Ca. Unfortunately, the situation is such that experimental data do not exist for some reactions of interest, and there are also sizable discrepancies between the data sets that are available in EXFOR.

We have measured cross sections up to 200 MeV for the reactions involved in PET range verification in order to improve the simulations of the expected activity distributions in the patient. There are eleven reactions of interest that produce either the long-lived isotopes via ¹²C(p,x)¹¹C, ¹²C(p,x)¹³N, ¹⁴N(p,x)¹¹C, ¹⁴N(p,x)¹³N, ¹⁴N(p,x)¹⁵O, ¹⁶O(p,x)¹¹C, ¹⁶O(p,x)¹³N and ¹⁶O(p,x)¹⁵O, or the short-lived isotopes via ¹²C(p,x)¹²N, ³¹P(p,x)²⁹P and ⁴⁰Ca(p,x)^{38m}K. These experiments have been performed at the CNA in Spain and WPE and HIT in Germany by means of three different detection systems (PET scanners, and NaI and LaBr₃ detectors). The

data have been obtained either by the multi-foil activation technique combined with a measurement with a PET scanner, or by single-foil activation and conventional detectors. A wide variety of strategies have been implemented to validate and ensure the accuracy of the results, and the new set of cross sections (measured for the first time for the short-lived ¹²N, ²⁹P and ^{38m}K) have been compared to previous data, evaluations and calculations.

The impact of these new cross sections for PET range verification has also been assessed by simulations of the β^+ production and activity profiles as a function of time for each isotope in tissue-equivalent phantoms, and for comparison with equivalent data calculated with the current evaluated data. These results illustrate the importance of new data, and the need for revised evaluations to obtain a reliable implementation of PET range verification. This is especially relevant for some of the reactions producing long-lived radioisotopes, but is of utmost importance for reactions producing the short-lived isotopes needed for online verification, since these are the first suitably produced cross-section data to date.

2.10. Measurements of Charged-particle Induced Reactions at NPI, ŘEŽ, O. Lebeda

The excitation functions of the proton- and deuteron-induced nuclear reactions on naturally monoisotopic gold have been measured by means of beams of the U-120M cyclotron and stacked foil technique [21, 22]. Detailed measurements of the theranostic pair ^{197m,g}Hg as a main product revealed inconsistencies in the decay scheme of ^{197m}Hg. This fact led us to undertake detailed measurements of a chemically-separated point source of carrier-free ^{197m,g}Hg by means of coaxial and planar HPGe detectors. The resulting decay data were provided to Kondev, who revised the decay scheme along with slight corrections to the half-life [23]. This in turn resulted in revisions to the originally measured cross sections, and other published decay data where appropriate [24].

Terbium radioisotopes have also attracted the attention of the nuclear medicine research community due to the existence of four radionuclides with either suitable therapeutic or imaging properties. As one of the former, ¹⁶¹Tb represents an interesting analogue to ¹⁷⁷Lu, although previously explored production routes do not seem to provide sufficient yields, except the neutron activation of ¹⁶⁰Gd. We decided to re-measure proton-induced reactions on ^{nat}Dy in order to investigate potential of the ¹⁶⁴Dy(p, α) reaction for the formation of ¹⁶¹Tb. The results confirmed the extremely low cross-sections of the ¹⁶⁴Dy(p, α) reaction, and therefore no practical importance for the ¹⁶¹Tb production. Cross sections for several other radioisotopes of Ho, Dy and Tb were also obtained [25].

Careful re-measurements have been made of the monitoring reactions for protons on titanium and copper [26], and ³He-induced reactions on monoisotopic ¹⁶⁵Ho and natural titanium [27].

As a therapeutic α emitter, ²²⁵Ac is attracting increased attention due to the significant potential of this actinide decay-chain in the targeted alpha therapy of metastatic cancer and small tumours. If internalized, most components of the decay chain emit α particles in the targeted cells without significant impact on the surrounding healthy tissue. The presence of four major α -particle emitters in the decay chain and the long half-life of ²²⁵Ac limit the patient dose to 8 MBq or less. However, a main hindrance of implementing ²²⁵Ac in clinical practice is limited availability, hence the recent exploration of various production routes. One promising alternative is the ²²⁶Ra(p,2n) reaction, for which there is only one existing measurement of the excitation function with cross sections at five proton energies [28], and no measurements of ²²⁶Ac as the only important radioisotopic impurity. This and other ²²⁵Ac production routes involve a contribution from ²²⁶Ra fission [29]. Under these circumstances, we are planning to measure the excitation functions of the proton-induced reactions on ²²⁵Ac in the near future.

2.11. Nuclear Data Needs for High Energy (p,x) Isotope Production and Evaluation, A. Voyles

When well-characterized experimental data on cross sections or isotopic yields are unavailable, the isotope production community and other users of such data rely upon predictive codes to provide estimates of their requirements [30]. At present there is no universal theory for the prediction of nuclear reaction cross sections, and therefore semi-phenomenological models must be parameterized and tuned to match the experimental data. Unfortunately for applications that include isotope production, the data for intermediate-to-high proton energies (> 50 MeV) and for deuterons, alpha particles and other light ions at all energies are relatively sparse, and there are only a small number of high-quality evaluations such as the IAEA charged-particle cross-section database for medical radioisotope production.

Collaboration has been established between Brookhaven, Lawrence-Berkeley and Los Alamos National Laboratories to help address the data needs within the US DOE Isotope Program for emerging isotope production pathways, and measure (p,x) reactions relevant to isotope production from threshold to 200 MeV for both the primary isotopes of interest and their impurities. Results from the TREND collaboration have been published for ⁷⁵As(p,x)⁶⁸Ge, ⁷²Se [31] and ${}^{93}Nb(p,x){}^{90}Mo$ [32, 33] and their impurities, and results for the ${}^{nat}Tl(p,x){}^{202}Pb$, $^{nat}Sb(p,x)^{119m,121m}Te$, and $^{nat}La(p,x)^{134}Ce$ reaction campaigns will be submitted shortly for publication. Each of these five campaigns have yielded measurements of 25-40 unique product channels spanning proton energies from 0 to 200 MeV, resulting in a significant amount of high-fidelity and internally consistent reaction data suitable for identifying and correcting deficiencies in the reaction modelling of these channels. Furthermore, TREND collaboration with Koning has involved systematic evaluations of (p,x) reactions based on the TALYS reaction-modelling code. While we are not claiming this process represents a formal evaluation, discrepancies have been revealed in the quasi-continuum nuclear statistical properties, particularly the modelling of nuclear level densities, proton and neutron optical model potentials, and pre-equilibrium secondary particle emission, which appear to be in part responsible for the lack of predictive capability in (p,x) reaction modelling [30]. Direct measurements of these observables as a function of excitation energy would greatly improve the performance of these codes, while providing simultaneous benefit to other application areas such as nuclear astrophysics. This modelling work has also revealed the potential dangers involved in the evaluation of a single reaction channel of interest: regardless of adopting a descriptive or predictive evaluation process, evaluations of experimental data based on a single reaction channel lead inherently to false minima for other channels that arise as a consequence of the constrained nature of the total cross section. This has a direct impact on neighboring reaction channels (such as for the production of contaminant radionuclides), and affects calculations in the planning of a production target [31, 32]. Model-based evaluations should be performed simultaneously on as many strongly-fed reaction channels as possible, including notable contaminants, to ensure that the recommended cross sections are physically selfconsistent. We further recommend that experimenters measuring cross sections for the production of emerging isotopes should report as many as possible of any observed competing channels, both to increase the body of experimental nuclear data as well as for inputs in future reaction evaluations. Finally, characterization of the production of stable nuclides and secondary particle spectra (particularly for secondary neutrons) need to be addressed by the community, particularly at the many high-energy (p,x) production sites around the world, owing to the profound impact of both of these products.

We also report several recommendations with broader impact for the isotope-production community. Observations during our recent TREND studies suggest that the recommended 2017 cross sections for the ^{nat}Cu(p,x)⁵⁸Co monitor reaction may be approximately 8% lower

above a beam energy of 100 MeV, in which this earlier evaluation is dominated by Michel et al. data [34] relative to several other strongly-fed reaction channels with EXFOR data. Additional measurements of this reaction channel need to be performed, leading to an updated evaluation of this channel in particular that is one of only three channels with an IAEA evaluation above 100 MeV. Furthermore, we recommend that existing IAEA evaluation channels where experimental data exist should have their evaluations updated beyond 100 MeV - several international production sites operate in this energy range, and require high-fidelity monitor data at such energies. We also propose that a new high-energy proton monitor reaction based on ⁹³Nb(p,4n)⁹⁰Mo be considered in the next IAEA evaluation cycle. Natural niobium is monoisotopic (⁹³Nb), readily available commercially at high purity, fairly chemically inert, and can easily be rolled into foils as thin as 1 μ m. ⁹⁰Mo is also sufficiently long lived ($\epsilon = 100\%$, $t_{1/2} = 5.56 \pm 0.09$ h) with seven distinct and strong gamma lines (notably the 122.370-keV [I_y = 64 ± 3%] and 257.34-keV [I_y = 77 ± 4%] lines) which can be easily used to quantify ⁹⁰Mo production [35]. ⁹⁰Mo is also completely immune to (n,x) production on ⁹³Nb, being produced only via the primary proton beam, whereby only the ${}^{90}Mo\gamma$ lines can be observed as daughter 90 Nb undergoes ε decay to stable 90 Zr. Our group has performed and published three measurements of this excitation function and all three studies observed competing reaction channels up to 200 MeV [31, 32, 33], with a further three imminent experiments along with additional EXFOR data already available that together lay considerable groundwork for undertaking a more comprehensive evaluation.

A fundamental requirement is a reliable evaluated repository of isotope production data, combining the rigorous evaluation methodology of current libraries such as the IAEA chargedparticle cross-section database for medical radioisotope production with the completeness of such libraries as TENDL. The ideal repository would be a comprehensive database offering evaluated recommendations of cross-section data for all direct channels of interest along with all relevant impurity and stable channels. Such a library would need to offer access to full sets of experimental data in addition to their recommended values, presented in both a format and structure tailored towards nuclear data users rather than just evaluators and generators. Therefore, we propose that nuclear data users and isotope producers be included as collaborators in this effort, along with other interested parties within the IAEA and developers of modern reaction modelling codes such as EMPIRE and TALYS. Along with recommended cross-section data, such a library should ideally contain integrated tools to calculate stopping powers, production yields, specific activities, cold metal yields, radionuclidic purity and dose rate estimates to assist in shielding and transport. Such a library would need to be accessible, transparent and flexible in order to respond rapidly to individual requests and the provision of updates – a library designed with user utility in mind.

With the possibility of potentially unquantified sources of correlation within the experimental cross sections and associated decay data, uncertainty propagation estimates in existing evaluations are likely to be incomplete. Therefore, covariance matrices adopted in future evaluations should be made available to nuclear data users upon their request. These matrices would include model correlations, as well as those arising from the fit to all experimental data that lead to the recommended cross-section values. Correlations arising from experimental data is a topic that has yet to be fully explored in the context of isotope production, and the US Nuclear Data Program is planning a recommended set of uncertainty templates for future isotope-production experiments, a task for which we are currently soliciting input and participation. Such covariances matrices could also be used to augment the power of future production planning tools, such as the use of Bayesian sampling to fold covariances for cross-section data and stopping powers into the calculation of reaction rates/yields, which is believed to offer to users more physically accurate yield calculations than other tools.

Additionally, the decay data for many nuclides of high relevance in applications are surprisingly not as accurate as they could be. Many radionuclides have uncertainties in their half-life of above 0.5% particularly for radionuclides with Z > 82, and are frequently based on less than three measurements dating back as far as the 1950s/1960s. Another issue affecting decay data is that gamma transitions often have > 1% uncertainties in their branching ratios, particularly for those γ emissions with energies below 150 keV that are heavily converted and result in large X-ray yields. These X-rays and competing Auger electrons are calculated by propagating outwardly the vacancies created by electron conversion. Our best tool for that purpose is the EADL database, which is a sub-library in ENDF/B that lacks uncertainty data and correlation information. The need for an updated EADL database has been identified as a top priority in other forums owing to the need to quantify the Auger electrons of significant interest in nuclear medicine. Electron vacancies created following electron capture and electron conversion are calculated by means of the BetaShape and BrIcc codes, respectively, but the fluorescence yields and vacancy transfer probabilities are lacking to calculate precisely the atomic radiation produced as these vacancies are filled. Recent advances in micro-calorimeter detector systems with much improved resolution over germanium detectors will also make the need for an improved EADL database even greater.

Finally, we wish to point out the long-standing issue of poorly-characterized charged-particle stopping powers at energies of interest to isotope production. Well-benchmarked charged-particle stopping powers (e.g., dE/dx) are critical for a wide variety of applications including optimized isotope production. These needs have been well-documented at a number of Workshops for Applied Nuclear Data Activities (WANDA), most recently in a dedicated stopping power session at WANDA 2022 [36]. Stopping powers themselves introduce covariances into the measured and modelled nuclear data that are most relevant to these applications, and routinely need to be compensated for in many cross-section measurement campaigns. The largest uncertainties in dE/dx are generally at the lowest relative velocity of the ion referred to as the Bragg peak where two different theoretical models from Bohr and Bethe show the greatest difference, and guidance from experiment is often lacking. Modern dE/dx models introduce missing physics, including atomic excitation of both the beam and the material, but require experimental data for benchmarking adjustments. Any optimization of these model parameters requires guidance from experiments at low energy/nucleon, and would greatly improve production planning, as well as cellular dosimetry studies.

2.12. Nuclear Medicine: Atomic and Nuclear Decay Data, 2022/2023, A.L. Nichols

During the course of various IAEA coordinated research projects from 1995 onwards, close to 100 radionuclides were considered with existing and potential diagnostic and radiotherapeutic applications in nuclear medicine. Unlike specific production cross sections, the decay data for the majority of these radionuclides are in good to very good condition. Nevertheless, a number of the commonly applied and proposed procedures may be judged as requiring further decay-scheme measurements to resolve certain known issues, as well as confirmation of existing significant features of their decay data. Such an assessment was initiated in 2022/2023 for consideration on this basis, with a paper published in the Diamond Jubilee issue of *Radiochimica Acta* [37]. Noteworthy features of this study and further data requirements are outlined below, with radionuclides of concern in bold print. Further details of lesser decay-data inconsistencies as well as requirements for confirmatory measurements can also be found in Ref. [37].

Diagnostic γ emitters and single-photon emission computed tomography (SPECT):

- internal-conversion electron measurements recommended for ⁹⁹Tc^m IT decay;
- Auger-electron measurements recommended for ⁶⁷Ga EC decay;
- ¹⁵⁵Tb 100% EC decay evaluated decay scheme does not include 36 observed γ rays: Total Absorption Gamma-ray Spectroscopy (TAGS) studies recommended;
- ¹⁹⁶Au 93.0(3)% EC decay and 7.0(3)% β⁻ decay → 7 or 8 EC transitions (mainly to 1st and 2nd excited states of ¹⁹⁶Pt), and 1 or 2 β⁻ emissions (primarily to 1st excited state of ¹⁹⁶Hg): energies and relative emission probabilities of seven of 15 known γ rays have been fairly recently measured [38], whereby data for lower-intensity 326.2-, 521.4- and 1091.4-keV γ rays exhibited various degrees of discrepancy with earlier studies merits confirmatory studies.

 β^+ emitters for positron emission tomography (PET):

- ⁶¹Cu 100% EC/ β^+ decay \rightarrow 12-13 EC/ β^+ transitions, with ground state to ground state dominant, and 35-39 gamma rays (three dominant): although possessing a reasonably well-defined decay scheme, recent extensive γ -ray studies require confirmation [20] along with additional β^+ experimental studies, prior to re-evaluation (see also Subsection 2.14);
- Further spectral studies of ⁶⁴Cu 61.5(3)% EC/ β^+ decay and 38.5(3)% β^- decay are merited: potential theranostic functions in the form of these two extremely simple decay modes within a single radionuclide \rightarrow two EC/ β^+ transitions with ground state to ground state dominant, and one β^- emission from ground state to ground state.

Non-standard β^+ emitters:

- ¹²⁴I 100% EC/β⁺ decay merits further γ singles and γ-γ coincidence measurements 24 EC/β⁺ transitions, mainly ground state to ground state, 1st and 10th excited states of ¹²⁴Te, with 74 gamma rays of which 602.73, 722.8 and 1690.96 keV are the most significant;
- -100% EC/β⁺ decay: ⁷⁶Br with 38 observed/unplaced γ rays, ¹²⁰I with 72 observed/unplaced γ rays, ¹²¹I with 48 observed/unplaced γ rays, and ¹⁵²Tb with 248 observed/unplaced γ rays TAGS studies recommended to determine need for more extensive γ singles and γ-γ coincidence measurements.

Palliative and therapeutic radionuclides:

- Parent-daughter ¹⁰³Pd 100% EC decay and ¹⁰³Rh^m 100% IT decay \rightarrow ¹⁰³Pd: four EC transitions and nine gamma rays, and ¹⁰³Rh^m: single gamma ray re-determine X-ray, internal-conversion electron, Auger-electron and γ -ray energies and emission probabilities to confirm recent studies [39, 40];
- 161 Tb 100% β^{-} decay X-ray and internal-conversion electron studies merited;
- ²²⁵Ac 100% α decay \rightarrow ²²⁵Ac with 14 observed/unplaced γ rays, and a further 21 of doubtful origin require extensive γ singles and γ - γ coincidence measurements.

Potential therapeutic radionuclides:

- ⁶⁷Cu 100% β⁻ decay → four well-defined β⁻ emissions and six gamma rays [41] measured and re-evaluated decay scheme to be incorporated into recommended international/national databases;
- ¹¹⁴In^m, 1γ, (1β⁻, 2γ); ¹¹⁷Sn^m, 3γ; ¹⁹³Pt^m, 3γ; and ¹⁹⁵Au^m, 5γ IT decay measurement/re-assessment of internal-conversion electron probabilities for radiotherapy;
- ¹³¹Cs and ¹³⁵La 100% EC decay potential sources of X-rays and Auger electrons for microdosimetry. Auger-electron and X-ray decay data calculated in both spectral and tabulated forms (BrIccEmis code, NS_RadList v1.0);

- ¹⁹⁷Hg^m 94.68% IT decay and 5.32% EC decay, and ¹⁹⁷Hg 100% EC decay \rightarrow ¹⁹⁷Hg^m: 94.68% IT decay 2 γ , 5.32% EC decay one EC, 5 γ ; and ¹⁹⁷Hg: 100% EC decay, three EC, 3 γ (both isomers identified with radiotherapy, and a joint source of X-rays and Auger electrons at the molecular scale [23] – re-evaluated decay schemes to be incorporated into recommended international/national databases.

Fully-accepted medical procedures are commonly undertaken jointly, as well as exclusively and uniquely: surgery, chemotherapy and radiotherapy. Well-defined and personalised LET therapeutic treatments are practiced: "tailoring the right therapeutic strategy for individual patients at the right time." And there are emerging treatments that perform as theranostic pairs (**thera**/peutic + diag/**nostic**), e.g., ${}^{86}Y(\beta^+)-{}^{90}Y(\beta^-)$, ${}^{132}La(\beta^+)-{}^{135}La(\gamma)$ and ${}^{68}Ga(\beta^+)-{}^{177}Lu(\beta^-)$, along with consideration of single radionuclides that emit intense lower-energy γ rays, along with suitable therapeutic radiation, e.g., ${}^{47}Sc$ and ${}^{67}Cu$.

Competition can be expected from on-going vaccine research that does not involve patient radiation, some already at the early stages of clinical trials: protein/peptide vaccines, DNA and RNA vaccines, whole cell vaccines, virus vaccines, etc. As for Machine Learning (ML) and Artificial Intelligence (AI), AI data accumulation and in-depth interrogation happens now in some forms of medical diagnosis. There is a need to debate the relative merits of subjective expertise versus objective decisions induced via $ML \rightarrow$ benefits or otherwise of subjective evaluations and the possibility of fully implementing objective AI.

2.13. Recent Developments of the Calculation of Auger-electron Yields from Medical Isotopes, *T. Kibédi*

The calculation of atomic radiations, Auger electrons and X-rays emitted by medical radionuclides can be very important for the treatment of certain cancers, and can also be used to assess the completeness of the proposed decay schemes of such radioactive isotopes. Short-range Auger electrons with high emission rates make them attractive in the development of tumour treatment strategies based on well-defined dosimetry calculations. Such patient specific approaches require a sound knowledge of the full energy spectrum at the nanoscale level.

BrIccEmis has been developed at the Australian National University to use the ENSDF file for nuclear decay input and the theoretical probabilities of electron capture and internal-conversion electrons taken from BetaShape [42] and BrIcc [43], respectively. Atomic transition rates are taken from EADL [44], while atomic transition energies are calculated by means of the RAINE code [45] with correction for QED and Breit effects [46]. The initial vacancy is propagated with a Monte-Carlo technique, until all vacancies reach the valence shell, or no transition is energetically possible.

A new database of precompiled atomic spectra has been produced to speed up the BrIccEmis calculations [46], and a computer tool entitled NS_RadList has been developed to access the data. Output from the calculations include a detailed report, and files of 1-eV binned spectra are produced. Extensive testing of the code is underway, and a detailed publication is in preparation for submission to Atomic Data and Nuclear Data Tables.

Recommendations:

- Compile experimental data on Auger electron yields, especially for the outer shells, in order to carry out benchmark calculations.
- Experimental ratios of KLL Auger-electron to conversion-electron intensities in order to benchmark theoretical atomic radiation rates. The accuracy of EADL has never been validated.

2.14. Review of Decay Data for ⁶¹Cu, F.G. Kondev

A review has been undertaken of the existing evaluations of ⁶¹Cu decay data [47, 48] for comparison with recently reported measurements of the relative γ -ray emission probabilities by Bleuel *et al.* [20]. These relative and absolute γ -ray emission probabilities in the β^+ /EC decay of ⁶¹Cu are presented in Table 3.

Eγ (keV)	relative I_{γ}			absolute	e Ι _γ (%)
	ENSDF2020 [47]	DDEP2013 [48]	Bleuel et al. [20]	ENSDF2020 [47]	DDEP2013 [48]
67.412(10)	31.6(10)	33.1(16)	N/A	4.0(6)	4.0(6)
282.956(10)	100(4)	100.0(24)	100	12.7(20)	12.0(17)
373.050(10)	16.8(4)	17.4(4)	16.9(2)	2.13(33)	2.09(30)
588.605(10)	9.2(1)	9.6(1)	9.57(17)	1.16(18)	1.15(16)
656.008(10)	82.0(14)	86.8(15)	79.3(10)	10.4(16)	10.4(15)
1185.234(15)	28.6(6)	30.1(6)	28.8(4)	3.6(6)	3.6(5)

TABLE 3. Relative and absolute γ -ray emission probabilities in the β^+ /EC decay of 61 Cu.

As illustrated in Table 3, there is good consistency between the recommended γ -ray data in ENSDF [47] and DDEP [48]. While there is a 5.9% difference between the relative I_{γ} for the 656.008-keV γ ray in ENSDF and DDEP, the absolute γ -ray emission probabilities are essentially the same. This is due to the fact that a number of γ rays contribute to the normalization factor (*NR*) that is used convert the emission probabilities from relative to absolute scale (*NR* x I_{γ} (rel) = I_{γ} (abs)):

$$NR = \frac{100 - I_{(\beta+/EC)}[g. s. to g. s.]}{\sum I_{\gamma}(rel) \times (1 + \alpha_T)}$$

where $I_{\gamma}(rel)$ are the relative γ -ray emission probabilities for those γ rays that directly feed the ⁶¹Ni ground state, α_T are their total electron conversion coefficients, and $I_{(\beta+/EC)}[g.s. to g.s.]$ is the direct EC-decay branch to the ⁶¹Ni ground state. Values of NR = 0.127(16) and 0.120(17) were determined in ENSDF [47] and DDEP [48], respectively, and these were used to obtain the absolute γ -ray emission probabilities in the decay of ⁶¹Cu. While the relative γ -ray intensities are accurate to about 1-2%, the uncertainties of the absolute γ -ray emission probabilities are much larger (in the order of 10-17%), due to the ~10% uncertainty in the direct β^+/EC decay branch to the ⁶¹Ni ground state.

Recent work by Bleuel *et al.* reported on the relative emission probabilities of several γ rays within the ⁶¹Cu decay scheme [20]. The relative intensities were obtained as a weighted average of values from about 107 individual measurements. For example, the measured I_γ(rel) values for one of the strongest 656.008-keV γ ray range between 63(8) and 87(8), relative to I_γ(rel) = 100 for the 282.956-keV γ ray, with a reported weighted average value of I_γ(rel) = 79.3(10) (see Table 3 and Ref. [20]). Although the authors of Ref. [20] claimed that this result would significantly impact the recommended decay data and excitation functions of the ^{nat}Ni(d,x)⁶¹Cu reactions, such a conclusion should be treated with caution given the lack of appropriate absolute γ -ray intensity data in Ref. [20]. As discussed above, the direct β^+ /EC decay branch to the ⁶¹Ni ground state needs to be determined with better precision, in order to improve the decay data for ⁶¹Cu. The results of Ref. [20] also need to be considered in future decay-data evaluations of ⁶¹Cu.

3. DISCUSSION AND REQUIREMENTS

Discussions were driven by advances in the field of nuclear medicine since the most recent studies by the IAEA-convened nuclear data community. The rate at which global regulatory agencies approve new diagnostic radiopharmaceuticals is increasing, and has expanded the portfolio of radionuclides used for positron emission tomography and single photon emission computed tomography imaging. Targeted radiopharmaceutical therapy is also rapidly expanding into clinical practice, and has increasingly been coupled to diagnostic technologies in "theranostic" applications. High dose rate "FLASH" radiotherapy has prompted a surge of interest in high-energy charged-particle reactions and posed new radiobiological questions. The global infrastructure that supports these efforts with radionuclide production has reacted with a proliferation of commercialized accelerator technologies, and the nuclear data community is responding with both new and improved data measurement efforts. This growth is expected to continue, necessitating not only further measurement and evaluation campaigns, but also concerted efforts to support (with training and policy advocacy) and disseminate nuclear data science to an increasingly diverse international community of users via focused topical and interdisciplinary exchanges, as well as the development and assembly of comprehensive and easily accessible databases.

This technical meeting followed several years of IAEA-supported consultant work to address the recommendations of a previous Technical Meeting on Nuclear Data for Medical Applications in 2018 that has been fully documented in IAEA report INDC(NDS)-0776 [6]. These efforts are described in two recent publications [7, 8], with two further papers published in late 2023 [9, 10]. The published evaluations are described and tabulated in Subsection 2.7, whereby the data are divided into PET, SPECT, therapeutic and monitor reaction categories as done previously. All new relevant data that became available after the 2018 report have also been added to the new evaluations.

3.1. Charged Particle-induced Reaction Data

New measurements are still required to address some of the recommendations of INDC(NDS)-0776 [6], several of which concern radionuclides being used in medical applications with human subjects. Furthermore, priorities are also ever-shifting as new radiochemical and pharmaceutical technologies generate compelling efficacy data, or reveal new issues that require nuclear data measurements and re-evaluations. Several important themes emerged from discussions to guide our future efforts in a focused manner, and these are summarized below.

3.1.1. Cases with Insufficient Measured Reaction Data

New noteworthy experimental studies arise from situations in which evaluations efforts are prevented by insufficient measurements. Along with the insufficiencies identified in Subsection 2.7, these discussions also noted a need for measurements of the following:

- reactions to produce ⁷⁰As, ⁷¹As and ⁷⁴As at low energies from germanium targets,
- reactions to produce ⁷²Se from ⁷⁵As targets, i.e., $^{75}As(p,4n)^{72}Se$ and $^{75}As(d,5n)^{72}Se$,
- proton- and deuteron-induced reactions to produce ¹¹⁷Sb and ¹¹⁹Sb from tin targets at low energies,
- reactions to produce ¹⁹¹Pt,
- potential monitor reactions that avoid the problem of secondary neutrons and consequent neutron-induced reactions at intermediate energies (50-200 MeV) – ^{nat}Nb(p,x) reactions were proposed for this purpose in Ref. [6].

ACTION: several therapeutic radionuclides of current interest should remain the subject of ongoing scrutiny in case of new measurements [6].

As a lower priority in the 2018 report, many reactions with insufficient measured data in the "intermediate" energy region between 40 and approximately 200 MeV were identified, which is within the energy range of an increasing number of radionuclide production facilities (including commercial 70-MeV cyclotrons). These data have not been considered in any known subsequent work. Several reactions previously evaluated require upward extensions in energy to 200 MeV, for example: ${}^{55}Mn(p,4n){}^{52}Fe$, ${}^{59}Co(p,3n){}^{57}Ni$, ${}^{68}Zn(p,\alpha n){}^{64}Cu$, ${}^{71}Ga(p,4n){}^{68}Ge$, ${}^{75}As(p,3n){}^{73}Se$, ${}^{85}Rb(p,3n){}^{83}Sr$, ${}^{88}Sr(p,3n){}^{86}Y$, ${}^{125}Te(p,2n){}^{124}Te$, ${}^{124}Xe(p,pn){}^{123}Xe$, ${}^{69}\text{Ga}(p,2n){}^{68}\text{Ge},$ $^{nat}Br(p,x)^{72}Se, {}^{68}Zn(p,2p)^{67}Cu$ 124 Xe(p,2p) 123 I, 45 Sc(p.2n)⁴⁴Ti. and 232 Th(p,x) 225 Ac.

3.1.2. Renewed Focus on Reactions that Produce Radioisotopic Impurities

As application of radionuclides previously foreign to the clinic becomes routine, their radionuclidic purity will naturally be subjected to increased scrutiny. Radioisotopic impurities are particularly important to minimize on the basis of a careful choice of nuclear reaction route, incident projectile energy and irradiation parameters because they cannot always be purified from the desired product with standard radiochemical techniques. One suggestion was to develop criteria for a systematic scan to identify side-channel reaction products based on the relative half-life of the impurities involved. Stable impurities are also of concern mostly at higher-beam energies for the molar activity of a final drug product targeting high-affinity receptor systems, especially in therapeutic applications where high activities are administered. The relevant reactions in many cases need evaluation, and in some cases new measurements may be required. Some reactions, for example (p,γ) and (n,γ) , are often omitted from consideration, but are nevertheless important to measure (e.g., in the production of ⁵⁵Co and ¹²⁴I). The threshold energy region of many impurity-producing reactions is especially important given the need to minimize the contributions of these reactions, but this energy region is often not given the dedicated experimental attention required for characterization with respect to the desired precision and accuracy.

Several example cases of radionuclides were identified whose production may be affected by the presence of impurities:

- production of 89 Zr from Y targets: 89 Y(p,2n) 88 Zr, especially near threshold,
- production of ⁴⁴Sc and ⁴⁷Sc from Ca and Ti targets: reactions that form ⁴⁶Sc and ⁴⁸Sc,
- production of ⁶⁸Ga from Zn targets: ${}^{66/67/68}Zn(p,x){}^{66/67}Ga$ reactions (some reactions that form ⁶⁶Ga have already been evaluated),
- production of 52g Mn: ${}^{nat}Cr(p,x){}^{54}$ Mn, ${}^{nat}Cr(p,x){}^{51}$ Mn and ${}^{nat}Cr(p,x){}^{51}$ Mn $\rightarrow {}^{51}Cr$,
- production of ¹⁵²Tb (β^+) and ¹⁵⁵Tb (SPECT) from Gd targets: reactions that produce ^{153/154/156}Tb,
- production of ⁸⁶Y from Sr targets: reactions that produce ^{85,85m,87,87m,88}Y,
- production of ⁵⁵Co from ⁵⁸Ni or ⁵⁴Fe: reactions that produce ^{56,57,58}Co,
 production of ¹¹⁷Sb and ¹¹⁹Sb from Sn targets: reactions to produce ^{118m,120m,122,124,125}Sb.

Following their respective evaluations, formal communication via established channels (e.g., the IAEA Medical Portal) should be revised to emphasize the importance of impurityproducing reactions in the production of the radionuclides in question. This concept of evaluated data dissemination was discussed at several points during the meeting, and was closely related to consideration of the multiple international attempts to consolidate various sources of nuclear data (cross sections, decay data, fission yields, etc.). The IAEA Medical Isotope Browser has some functional connectivity to evaluated nuclear decay data and also includes TALYS theoretical predictions of reaction cross sections and prior reaction evaluations. Future data evaluations should continue to be incorporated into these online tools.

ACTION: The IAEA NDS should coordinate an iterative scan to create a comprehensive list of possible impurity radionuclides as additional candidates and explore methods of including this data in online tools for users.

3.1.3. Validation of Reaction Data with Integral Yield Measurements

Yield measurements are an essential validation of measured nuclear reaction data [6], and are especially valuable in the selection of incident and exit beam energies along with target synthesis parameters. A great deal of this validation is possible using targets of natural isotopic abundance, and experiments can often be performed by irradiating multiple-target materials simultaneously, reducing cost and uncertainty simultaneously. Methodological reproducibility is paramount in these measurements, and experimental verification of the incident energy, target characterization, target beam intercept, and low-beam intensities are essential for accurate quantification. Ideally, these measurements are best conducted using a suitable range of incident particle energies available on commercial accelerators and cyclotrons. Measuring product activity ratios may offer an additional means to constrain the results compared to absolute yield measurements of a single product. For example, the $^{nat}Cu(p,x)$, $^{nat}Cu(d,x)$ and $^{nat}Ni(d,x)$ reactions each produce multiple zinc and copper radionuclides with easily distinguishable products. Finally, in some cases it may be important to coordinate the expert contribution of a laboratory experienced in quantitative radiochemical techniques to obtain samples that can inform high-precision yield measurements independent of interferences in characteristic emission energies.

3.2. Neutral Particle-induced Reactions

Gamma- and neutron-induced reactions both retain recognized importance in the production of a small number of radionuclides, which are nevertheless in high demand in the medical community (e.g., ⁴⁷Sc, ⁶⁷Cu and ²²⁵Ac, see Table 4), and there is relatively little energy dependent data available to inform an optimal choice of accelerator parameters. This is also true as far as impurities are concerned, as mentioned in Subsection 3.1.2 for charged-particle induced reactions. Photon-induced reactions are of increasing importance because of the installation of multiple rhodotron machines in the United States of America and Europe, at least one of which has produced and introduced large (TBq) batches of ⁶⁷Cu into the marketable inventory. Reactions on converter materials are also of interest. Compilations of these and other reactions are maintained by the US DOE and IAEA-NDS (e.g., IAEA CRP on photonuclear reactions, with the recent release of the IAEA photonuclear reaction database IAEA/PD-2019, see web page https://www-nds.iaea.org/photonuclear/).

Product	Neutron-induced reactions	Photon-induced reactions	Impurity-producing reactions
⁴⁷ Sc	${}^{50}\text{Ti}(\mathbf{n},\alpha){}^{47}\text{Ca} \rightarrow {}^{47}\text{Sc}$	⁴⁸ Ti(γ,p) ⁴⁷ Sc	⁴⁷⁻⁵⁰ Ti(γ,x) ^{46,48} Sc
	$^{47}\text{Ti}(n,p)^{47}\text{Sc}$		⁴⁶⁻⁵⁰ Ti(n,x) ^{46,48} Sc
⁶⁷ Cu	70 Zn(n, α) 67 Ni \rightarrow 67 Cu	⁶⁸ Zn(γ,p) ⁶⁷ Cu	n/a
	⁶⁸ Zn(n,pn) ⁶⁷ Cu		
	${}^{67}Zn(n,p){}^{67}Cu$		
²²⁵ Ac	226 Ra(n,2n) 225 Ra $\rightarrow ^{225}$ Ac	226 Ra(γ ,n) 225 Ra $\rightarrow ^{225}$ Ac	226 Ra(n, γ) 227 Ra \rightarrow 227 Ac
		226 Ra(γ ,p) 225 Fr $\rightarrow ^{225}$ Ra $\rightarrow ^{225}$ Ac	

TABLE 4. Some neutron- and photon-induced reactions of interes	t.
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Neutron-induced reaction data at intermediate and high energies (> 14 MeV) also remain an important need. Relatively few facilities exist that can operate in this beam-energy range, especially with quasi-monoenergetic neutrons. These data are important to spallation sources

that produce large fluxes of secondary neutrons, to interstellar dosimetry, and fusion energy materials development, amongst others. The potential of accelerator-driven neutron sources has been increasingly realized in commercial and research settings, with fluxes that approach practical application parameters.

3.3. Theoretical Models

The main interaction between experimental data and the models is the use of measured and evaluated data to benchmark and improve model parameterizations of the nuclear reaction data. Theoretical calculations are useful in the evaluation of cross sections because they predict the yields of the impurities along with those of the desired product, and the reliability of the codes have improved in recent years (for example, predictions of (p,n) reactions in the worst cases have ~30% uncertainties at the peaks of their excitation functions). Iterative interactions between code developers and the experimental nuclear data community should continue to be facilitated by policy-making efforts and the various funding agencies. This requires that databases are available to users, and to this end the IAEA-NDS should make the complete EXFOR database computationally accessible to automated query by other suitably developed codes. This concern has been addressed by the NDS distributing EXFOR in C5, X5json and X4Pro/SQLite for download from the website (<u>https://nds.iaea.org/cdroms/#c5</u>), where brief descriptions of these products can also be found.

3.4. Measurements and Evaluations of Decay Data

Measurements are increasingly important for emerging therapeutic dosimetry by means of positron and single-photon emitters. Various decay-data requirements identified in IAEA report INDC(NDS)-0776 still remain unaddressed [6], along with recent related measurements [11, 20, 23, 39, 40] and various forms of in-depth review that have arisen since the IAEA meeting in December 2018 [30, 37]. Under such circumstances, new needs have been recognized in recent years for the following diagnostic radionuclides:

- ⁵¹Mn, ^{72,74}As, ¹³⁴Ce/¹³⁴La and ¹⁵²Tb are identified as positron emitters with high priority because of their progression towards clinical applications.
- ⁴³Sc, ⁵⁷Ni, ⁶⁶Ga, ⁷⁶Br, ⁸¹Rb, ^{82m}Rb, ⁸³Sr, ⁹⁵Ru, ¹²⁰gI, ¹²¹I, and ¹⁴⁰Pr are identified as lower priority positron emitters whose need for evaluation should be re-assessed in the event of any new relevant measurements.
- Further measurements of the 1345.77-keV γ line of ⁶⁴Cu are recommended because of the low absolute intensity (0.472(4)%). Furthermore, recent unpublished measurements at FZJ have furnished a value which is discrepant to that currently accepted.
- ¹²⁴I merits further γ singles and γ - γ coincidence to develop and confirm the decay scheme.
- A recent measurement of the positron intensity of ⁸⁶Y by FZJ is inconsistent with the accepted value and needs to be resolved.
- Single photon emitting radionuclides for SPECT that have been flagged for reassessment to determine the need for re-evaluation: ¹²³I and ¹⁵⁵Tb.

The decay data of several therapeutic radionuclides were also flagged for assessment in the 2018 report, including the beta-emitting radionuclides ⁴⁷Sc, ⁶⁷Cu, ⁷⁷As, ¹⁶¹Tb, ¹⁶⁷Tm and ¹⁷⁵Yb, and alpha-emitting ¹⁴⁹Tb.

Auger-electron emitters represent a class of radiation for which special nuclear data requirements exist. Certain production needs have already been covered in the reports from individual institutions (Section 2, above). Some Auger emitters require the evaluation of their nuclear decay data (e.g., as input to the BrIccEmis code). There is also a need to establish mechanisms/methods for the use of the decay data being generated by BrIccEmis, especially

codes such as GEANT4 and Penelope which themselves employ low-energy electron emission data. There is a separate need for experimental benchmarking and validation of the Auger-electron decay data calculated by BrIccEmis. Finally, comprehensive Auger-electron emission code predictions require dissemination. The previous technical meeting in December 2018 identified the following Auger emitters as meriting new measurements and targeted code-prediction studies [6]: ⁶⁷Ga, ⁷¹Ge, ^{103m}Rh, ¹¹⁹Sb, ¹³⁵La, ^{165,169}Er, ^{197m,g}Hg, ¹⁹¹Pt, ^{193m}Pt and ^{195m}Pt. There is a specific need for assessments of the conversion-electron intensity data of a number of additional radionuclides, that would be beneficial as input to the BrIccEmis code: ^{114m}In, ^{117m}Sn, ^{193m}Pt and ^{195m}Au. Finally, five specific requirements were also identified:

- ^{197m}Hg (95.68% IT decay and 5.32% EC decay) and ¹⁹⁷Hg (100% EC decay): a decaydata issue concerning the 13/2+ isomer has been resolved [23]. There is a need to ensure the adoption of these new data and their transfer to the database.
- Recent measurements of ¹⁰³Pd and ^{103m}Rh decay data have revealed a discrepancy that merits experimental resolution and subsequent re-evaluation of the full parent-daughter decay scheme [39, 40].
- New electron measurements of ^{99m}Tc are needed to confirm the absolute yields of the Auger and conversion electrons for validation of the output from BrIccEmis.
- ²⁰¹Tl electron-capture decay contains significant but uncertain EC transitions to the ground and 1st excited states. This radionuclide has potential as an Auger-electron emitter that is currently limited by chemistry issues. Tremendous production capacity exists this radionuclide is used commercially for SPECT, and is available worldwide.
- Additional γ -ray measurements along with structure and decay-data evaluation are merited for ¹²³I (both as a γ -emitter and for potential use in Auger-electron radiotherapy).

3.5. External Beam Therapy

As in previous CRPs and IAEA technical meetings, brief discussions of the nuclear data needs for hadron therapy were also conducted. The perceived priority is highest for more commonly used proton-beam therapy, high for carbon beams in current use and ⁴He beams soon to enter into clinical application, and lower for prospective beams (e.g., ¹⁶O beams and radioactive beams, such as ¹¹C and ¹⁵O). Data relevant to proton beams remain more highly prioritized than that for other prospective charged particles owing to the significant commercialization and wider proliferation of the former – the reader is referred to IAEA report INDC(NDS)-0776, and the references therein [6].

3.5.1. Proton-beam therapy

Beam-range verification via prompt gamma imaging requires gamma production cross sections (p,x γ), especially for ¹²C, ¹⁴N, ¹⁶O and perhaps for other targets (e.g., ^{nat}P and ^{nat}Ca). Evaluations of the measured data for proton-beam energies < 85 MeV are merited, along with the need for new measurements up to 250 MeV. Integral and energy differential (incident proton and emitted photon) data on prompt gammas up to microseconds have been requested by physicists involved in shielding and dosimetry calculations, as well as cross sections and branching ratios.

Beam-range verification via PET imaging has recently resulted in new cross-section measurements of reactions to produce positron emitters [49, 50]. As such, further additional measurements are still worthwhile for independent comparisons with the newly published data, although this is now seen as a lower priority than was considered to be the case five years ago. However, some unstudied reactions may still be of some importance, e.g., on targets of ¹⁶O, while noteworthy needs remain identified with the ^{nat}P(p,x) and ^{nat}Ca(p,x) reactions.

Target fragmentation as a function of beam energy and angle for proton-induced reactions was highlighted for necessary study, namely for biological dose modelling with an increasing interest to move from a fixed to dynamic RBE.

3.5.2. Carbon beams

Production of ¹⁰C, ¹¹C, ¹³N and ¹⁵O positron emitters up to 200 MeV/nucleon – all data involving ¹²C and ¹⁶O targets, fragmentation of the primary beam to produce positron-emitting residuals, and heavy-recoil projectiles (⁸B, ¹⁰C and ¹¹C).

3.5.3. ⁴*He beams*

Improved cross sections are required to produce 11 C, 13 N and 15 O positron emitters up to 200 MeV/nucleon. More accurate data have been requested on projectile fragmentation as a function of energy and angle at therapy energies (200 MeV/nucleon) and up to ~ GeV energies for radiography.

3.5.4. Other relevant statements

Neutron production by proton interaction on light elements (such as Al) was judged to be an important requirement for proton therapy, spacecraft and glass in microscopes. With new developments in proton therapy (e.g. FLASH and arc therapy), the need for passive elements in the beam is increasing (e.g., collimators, range shifters, bolus and other accelerator components). The quantification of these reactions and neutron production are currently deficient, and therefore such studies are recommended.

The possibility of future radioactive beams was noted, and requests for data on the interaction of, e.g., ¹¹C or ¹⁵O, with physiological targets can be anticipated. Oxygen-ion beams are also being explored for clinical usage. The need for studies on target and projectile fragmentation and relevant PET monitoring channels is foreseen under such emerging circumstances.

4. CONCLUSIONS

This technical meeting followed on from concerted efforts undertaken between 2012 and 2017 via an IAEA Coordinated Research Project, subsequent re-assessments at an IAEA technical meeting in December 2018, and recent IAEA-coordinated consultant efforts that remain ongoing. Recommendations have been made after consideration of both existing clinical needs and future directions that might be pursued in terms of on-going published research within the field of nuclear medicine. The expertise of those attending this 2023 technical meeting resulted in the identification and subjective prioritization of the needs for both nuclear-reaction and decay-data measurements and evaluations that would benefit the medical application of a relatively wide range of radionuclides.

All prior IAEA meetings and projects have resulted in the dissemination of new evaluations and recommendations via peer-reviewed forums, and ensured the incorporation of their products into publicly-available databases that are widely used across the nuclear data, radionuclide science and nuclear medicine communities (amongst other related bodies). The databases developed by IAEA Nuclear Data Section staff to disseminate the recommended excitation functions and atomic and nuclear data that have arisen constitute the standard resource for application-oriented technical users, and can be accessed at:

https://nds.iaea.org/medportal/

A recommended cross-section database for charged-particle monitor reactions is available at: https://nds.iaea.org/medical/monitor_reactions.html

A recommended cross-section database for the production of gamma emitters is available at: https://nds.iaea.org/medical/gamma_emitters.html A recommended cross-section database for the production of positron emitters is available at: https://nds.iaea.org/medical/positron_emitters.html

A recommended cross-section database for the production of therapeutic isotopes is available at: <u>https://nds.iaea.org/medical/therapeutic.html</u>

As emphasized previously, the maintenance, extension, and improvement of these datasets at regular intervals in the future is among the highest priority needs of the nuclear data community, and constitute a most important contribution of the IAEA-NDS to the field.

IAEA staff are urged to consider the recommendations outlined below in terms of the atomic and nuclear data needs for medical radionuclides over the next five to ten years. An attempt was also made to prioritize the various potential data requirements identified as important over the specified timescale stretching beyond 2030. Plans for appropriate work programmes to develop and improve such atomic and nuclear data over this same timescale should involve serious note being taken of the requirements and recommendations contained in detail throughout Section 3 above.

5. RECOMMENDATIONS

- 1) Support and prioritize acquisition of the following measured reaction and decay data of specific clinical radionuclides:
 - ²²⁶Ra(p,2n)²²⁵Ac reaction requires new measurements and resolution of observed discrepancies in the quantification of the gamma-ray emissions of daughters at equilibrium.
 - ⁶⁴Cu positron and 1345.77-keV gamma-ray intensities require new measurements to resolve discrepancies.
 - ⁸⁶Y positron intensity requires new measurements to resolve discrepancies.
 - ¹²⁴I positron intensity requires new measurements to resolve discrepancies.
 - ^{99m}Tc decay data requires new evaluation as support for Auger-electron calculations.
 - Need for new measurements and evaluation of reaction and decay data for ^{72,74}As and ¹⁵²Tb; such data for ⁵¹Mn should also be re-assessed.
 - ¹⁶¹Tb Auger yield and multiplicity, X-ray and conversion-electron data require assessment to determine the need for further measurements and evaluation.
 - Decay data of ^{149,152,155}Tb are complex, and should be assessed on the basis of potential usage to determine if there is a need for new measurements and/or evaluations.
- 2) Identify and include reactions that can produce problematic radioisotopic impurities in current and future measurements and evaluations of nuclear reaction data, and prioritize such radionuclides identified in Subsection 3.1.2 above. Incorporate these reactions into the online tools of the IAEA Medical Portal and associated webpages.
- 3) Current and future measurements and evaluations should include the validation of cross sections with measurements of integral target yields.
- 4) Add uncertainties to the absolute gamma-ray intensities reported in the evaluated reactions decay-data tables of the IAEA Medical Portal. This information is already available in the associated peer-reviewed publications.
- 5) IAEA should consider the organization of an international meeting on nuclear reaction and decay data that are required in microdosimetry and Monte-Carlo calculations to characterize the Auger-electron emissions.
- 6) Visibility and adoption of nuclear data evaluations remain infrequent and inconsistent within nuclear physics research, industry and nuclear medicine. Members of the nuclear data community and supporting organizations (such as the IAEA) should engage leading users in these fields starting with the Society for Nuclear Medicine and Molecular Imaging, the European Association of Nuclear Medicine and Molecular Imaging, and the

Society for Radiopharmaceutical Science to emphasize the importance of nuclear data to application-orientated work by collaboratively organizing special symposia at regular meetings and supporting joint endeavours that incorporate nuclear data in related studies.

- 7) Given the dramatically increased proliferation of accelerators and cyclotrons worldwide, there is a commensurate need for increased training and education of a skilled supporting work force. Under these circumstances, the IAEA should further enhance support for appropriate workshops (e.g., at ICTP in Trieste, IAEA headquarters in Vienna, and regionally-sponsored workshops), other training opportunities, and gatherings that consist of both young and experienced mentoring scientists, with special emphasis on the continued maintenance and development of highly necessary nuclear data expertise.
- 8) Ensure that the complete EXFOR database is computationally accessible to automated query by other suitably developed codes.

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Technical Meeting on Nuclear Data for Medical Applications

IAEA, Vienna, Austria 28-31 August 2023 Meeting Room M5 (hybrid)

Adopted Agenda

Lunch breaks 13:00–14:00, coffee breaks as needed

Ν	Ionday 28 August, 9:30–17:30					
	Opening of the meeting, A. Koning (Section Head NDS)					
	Election of Chair and Rapporteur(s), adoption the Agenda					
	Introduction, R. Capote (Scientific Secretary)					
	Participants' Presentations (~30'):					
	 Nuclear Data Research for Development of Novel Medical Radionuclides, S. Qaim 					
	 Extension of recommended cross section data base for production of therapeutic isotopes and charged particle monitor reactions, <i>F. Tarkanyi</i> 					
	 Cyclotron-production of Innovative Radionuclides: Nuclear Data Research Activities at the INFN-LNL, G. Pupillo, L. Mou 					
	 Production yields of ⁶⁴Cu and ⁶⁷Cu, Y. Nagai 					
	 TALYS for charged-particle cross sections: predictive power and parameter fitting, 					
	A. Koning					
	 Model considerations related to data for "Sc production from enriched titanium targets, and for ¹⁵⁵Tb production from enriched gadolinium targets. <i>L. Canton</i> 					
Τι	uesday 29 August. 10:00-18:00					
	Participants' Presentations cont'd (~30'):					
	 Input, output and lessons learned: PET and SPECT evaluations based on TM-Vienna 2018, 					
	A. Hermanne					
	Nuclear Data Needs for Medical Radionuclide Producers, J. Engle					
	 A new set of cross sections to produce beta+ emitters (¹¹C, ¹²N, ¹³N, ¹⁵O, ²⁹P and ^{38m}K), C Guerrera Sanchez (remeta) 					
	 Cross-section measurements for emerging therapeutic radionuclides with special regard to 					
	²²⁵ Ac, <i>O. Lebeda</i>					
	– Nuclear Medicine: Atomic and Nuclear Decay Data, 2023, A.L. Nichols (remote)					
	 Recent development of the calculation of Auger electron yields from medical isotopes, 					
	I. KIDEAI Deceny data of ⁶¹ Cy. E. Kondoy					
	 Decay uata of Cu, r. Kondev Nuclear Data Needs for High-Energy (n.x) Isotone Production & Evaluation 					
	A. Voyles (remote)					
	19:00 Dinner at a Restaurant (separate information)					
N	Wednesday 30 August, 10:00-18:00					
	Discussions and Drafting of the Meeting Summary Report					
	Review of nuclear data needs					
T	Thursday 31 August, 10:00-15:00					
	Discussions and Drafting of the Meeting Summary Report cont'd					

Technical Meeting on Nuclear Data for Medical Applications 28-31 August 2023, IAEA, Vienna

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Meeting participants at the IAEA Conference Center

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