Consensus nomenclature rules for radiopharmaceutical chemistry

– setting the record straight –

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These recommended guidelines were assembled by an international and inter-society working group after widespread consultation with peers in the wider field of nuclear chemistry and radiopharmaceutical sciences.

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Contents page

Preface 2
Scientific concepts, definitions, IUPAC rules and SI-derived units 3
Measurement of radioactive decay 3
Specific activity and molar activity 4
Apparent and effective specific activity resp. molar activity 4
'No-carrier-added', 'carrier-free' and 'carrier added' 5
Radionuclide and radioisotope descriptors 5
Radiochemical yield (RCY) 8
Definition of radiochemical yield (RCY) 8
Definition of activity yield (AY) 10
Definitions of purity 10
Physical units 11
Acknowledgements 12
Appendix 12
A) *Some Definitions from IUPAC Nomenclature Documents* 12
B) *Definitions and Units of Radiological Quantities* 14

Preface

The primary function of nomenclature is to ensure that spoken or written scientific terms and concepts leave no ambiguity in their interpretation. The ultimate intent of generating consensus nomenclature is therefore to create common conventions for terms and definitions, enabling effective and unambiguous communication and understanding within a scientific community. In order to achieve these goals, the international natural science community agreed to abide by and adopt the use of SI-derived units (1960) and IUPAC rules for chemistry (1921) (SI - International System of Units; IUPAC - International Union of Pure and Applied Chemistry). As the field of radiopharmaceutical chemistry is part of this wider community, it behoves us also to adopt these conventions: to ignore this would be impractical.

Over recent years, within our community of radiopharmaceutical sciences, there increased an incidence of incorrect usage of established scientific terms and conventions, and even the emergence of 'self-invented' terms. In order to address these concerns, an initiative was triggered by the 'Drug Development Committee' (DDC) of the 'European Association of Nuclear Medicine' (EANM). A Working Group on '*Nomenclature in Radiopharmaceutical Chemistry and related areas*' was established in 2015 to achieve clarification of terms and to generate consensus on the utilisation of a standardised nomenclature pertinent to our field. The members are active insiders of relevant scientific societies, e.g., EANM, 'Society of Radiopharmaceutical Sciences' (SRS), 'Society of Nuclear Medicine and Molecular Imaging' (SNMMI), 'Society of Radiopharmacology' (SRP) and respective national societies.

After conducting a worldwide survey by a questionnaire, aims of primary importance were agreed, and the WG produced a summary of its initial recommendations. These were used as 'guidelines to authors' for the submission of abstracts for the ISRS 2017 meeting. Other societies have also responded positively to using this summary as guidelines for future abstract submissions at their meetings. In addition to the summary document, a full text was prepared by the WG and was presented on the home page of the Society of Radiopharmaceutical Sciences in a wider context by the end of 2016, requesting comments from all peers in the field.

Following a period of open consultation, in order to gain feedback about the proposed recommendations and to discuss any further issues requiring clarification, all comments and views expressed during the consultation period on the posted nomenclature recommendation document were solicited and discussed within the working group. The resulting consensus is now incorporated into a pre-final document, posted on the SRS website, and any open or outstanding issues will be discussed at the 22nd ISRS meeting in Dresden (May 14th – 19th, 2017). Thus, we kindly request you to send any further comments on the newly posted document to Heinz H. Coenen (h.h.coenen@web.de) and/or Antony Gee (antony.gee@kcl.ac.uk) before 13 May 2017.

Subsequently, the resulting consensus nomenclature guidelines will be published in an appropriate journal as a reference source for the field, and as a basis for discussion and harmonising with publishers, editors, IUPAC, pharmacopeias, and key stakeholders beyond our immediate peer group.

Scientific concepts, definitions, IUPAC rules and SI-derived units

Below are summarised a number of terms (and descriptions thereof) of relevance to radiochemistry and related fields, which are already described and agreed by the wider scientific community, but are often used incorrectly in the literature. (for IUPAC see: https://iupac.org/what-we-do/nomenclature/ and for SI Units see: http://physics.nist.gov/cuu/Units/index.html).

These are complemented by other terms, not described by international convention, but that have been adopted within our field and which have prompted discussion with a cross-section of experts within the field of nuclear and radio-chemistry in order to clarify and enhance the unambiguous communication of scientific findings and research results within the community.

Measurement of radioactive decay

'Radioactivity' is defined as the property of certain *nuclides* showing *radioactive decay (*M. de Bruin: "Glossary of terms used in nuclear analytical chemistry", Pure Appl. Chem., **54**, 1533-1554 (1982); *Nomenclature for Radioanalytical chemistry*, Pure Appl. Chem.*,* **66**, 2513 - 2526 (1994), and as such, 'Radioactivity' is not a quantity or measure.

“Activity” and its SI derived unit, defined as the “Becquerel”, are the agreed terms for the quantity and measurement of the phenomenon of radioactivity.
Thus, Bq (MBq, GBq etc.) should be used as units for measurement of the activity of radionuclides, while pre-SI units (e.g., imperial units, like mCi, Ci) can be placed in parentheses after the stated SI derived units (see table in Appendix).

N.B.: In practice, it should not be a problem to also use the term “radioactivity” as long as it refers fully to ‘*activity of disintegration of a radionuclide*'. However, care should be taken, when merely using the term ‘activity’ in non-exclusively nuclear or radio-chemical contexts, as it may cause confusion with other terms such as ‘chemical activity’; e.g., of ligand binding, enzyme action, etc. (see also the description of ‘activity coefficient’ in standard Physical Chemistry text books).

Generally, the prefix “radio” indicates a context relating to the phenomenon of radioactivity, e.g. “radiochemistry”, or in combination with analytical methods, where it also denotes the measurement of radiation in addition to other spectroscopic signals, e.g., “radio-HPLC or radio-TLC”.

The often-used lab-jargon “hot” and “cold” must not be employed instead of the correct terms “radioactive” and “non-radioactive”, respectively, in formal public presentations, manuscripts or official documents.

Specific activity and molar activity

According to SI convention, the term 'specific' refers to a physical property as a function of the mass of the material in question; e.g., the specific heat capacity is the heat capacity of an object per kg of mass. Since in chemistry the amount of material (mass) is most often denoted in moles, related chemical properties are indicated in 'molar' units; e.g., molar volume. Because of this possible source of confusion, the following terms are to be used correctly (see Appendix):

Specific activity - the measured activity **per total amount in gram** of compound present; measured in Bq/g or GBq/mg etc.; symbol: $\mathbf{A_s}$.
Molar activity - the measured radioactivity **per total amount in mole** of compound; measured in Bq/mol or GBq/µmol, etc.; symbol: $\mathbf{A_m}$.

Besides in the occasional situation, where the molecular weight cannot be determined, or in the context of radionuclide development (such as the activity of irradiated target material), the term 'molar activity' is to be used instead of the term 'specific activity'.
Due to radioactive decay, the measurement time for the specific activity or molar activity determination must be stated; e.g., 'the specific activity was 50 GBq/mg' or 'the molar activity was 50 GBq/µmol' 2 h after the end of nuclide production, at the end of synthesis, at time of administration, etc.'

Apparent and effective specific activity resp. molar activity

In cases where amounts of other material are present in a radiolabelled compound preparation, the measured specific or molar activity is lower than the true value. This often happens if non-labelled materials present in the synthesis mixture are not entirely removed from the labelled product during purification. Examples are precursor molecules (e.g., spiperone) or a complexing ligand (e.g., DOTA-TATE), which have not been fully removed during the final product purification (e.g., [*N-methyl*-^{11}C]spiperone or [^{177}Lu]Lu-DOTA-TATE) after methylation or complexation, respectively, but also any other chemically different impurity.
In such cases, the terms apparent specific activity or apparent molar activity also take into account the amounts of the labelled and non-radiolabelled impurities (using moles, or weight, respectively).

An additional term used in this context is "effective specific or molar activity". This addresses the chemically, biologically or pharmacologically 'active' fraction of radioactive and non-radioactive materials. The term is often used to consider other (unkown) material present in a sample prepared, competing with the labelled product in its chemical or biological reactions, for example a complexation process or the binding to a target protein. In this case, however, the "effectivity" must be determined by an additional analytical process (e.g., receptor or enzyme binding assay, etc.), since it is not simply described by the measured "activity per total amount (quantity or mass) of material".

The term "pseudo" specific/molar activity must not be used, since the impurity has not been intentionally added.

'No-carrier-added', 'carrier-free' and 'carrier added' (see also Appendix A)

Since labelled compounds are generally mixtures of an isotopically unmodified compound and isotopically substituted compound(s) (see Appendix), the non-quantitative terms "carrier-free" (c.f.), "no-carrier-added" (n.c.a.) and "carrier-added" (c.a.) are often used as a general indication of specific/molar activity levels. These terms have already been adequately defined by A.P. Wolf (J. Label. Compd. Radiopharm. **18**, 1-2 (1981)), intensively discussed by de Goeij and Bonardi (J. Radioanal. Nucl. Chem. **263**, 13-18 (2005) and in the IUPAC draft of 2014 by Bonardi et al.

It is advised, however, that, the term "carrier-free" should only be used in cases, where an analytical verification has proven this state, i.e., that the theoretical specific or molar activity (absence of all other than specified isotope) is reached. As Eckelman, Volkert and Bonardi (Nucl. Med. Biol. **35,** 523–527 (2008)) and Lapi and Welch (Nucl. Med. Biol. **40**, 314-320 (2013)) pointed out, the routinely used radionuclides (e.g., ^{11}C, ^{18}F, ^{99m}Tc, ^{123}I, etc.) are never "carrier-free".

Thus, it is recommended to generally avoid the term "carrier-free" altogether.

N.B.: While 'carrier-free' implies 'no-carrier-added', the reverse is not true!

Radionuclide and radioisotope descriptors

The enrichment of a chemical compound with an isotope (stable or radioactive) of one or more of the elements of which it is constituted, is indicated by the symbol of the element, together with its mass number (as superscript in front), in square brackets immediately (i.e. with no hyphen or space!) preceding the compound's name or chemical formula; e.g., [^{2}H,^{14}C]benzene, or [^{2}H,^{14}C]$C_6H_{6,}$ for benzene enriched or labelled with stable deuterium and radioactive carbon-14 (see Appendix A).

N.B.: In a manuscript, the square bracket containing the radionuclide descriptor "[^{A}E]" should always be kept intact at the end of a line of text. If a full radiolabelled compound name needs to be fragmented at the end of a line of text, a hyphen may be placed after the square bracket and the remainder of the radiolabelled compound description continued on the next line. This is the only occasion a hyphen can be placed directly after a "[^{A}E]" square bracket.

The symbol for isotopic enrichment [^{A}E] should always be treated like a syllable, why in given case it should be hyphenated at the end of a line.

If a symbol of an element is given in a chemical formula, or in combination with the name of a chemical compound, together with a mass number "**^{A}E**", but without square brackets, according to IUPAC (see Appendix A), this indicates an isotopically substituted compound, having a composition such that all molecules of the compound only consist of the indicated (radio)nuclide. This means that the theoretical specific or molar activity of the atom or compound is attained; i.e., it is strictly 'carrier-free', a state rarely achieved in practice (see 'specific/molar

activity' above).

Examples of correct and incorrect descriptions of isotopically labelled compounds:
L-[^{13}N]alanine is correct;
[^{13}N]L-alanine, L-^{13}N-alanine or L-[^{13}N]-alanine are incorrect!
More detailed rules for designating labelling positions (e.g., L-[*methyl*-^{11}C]-methionine or L-[*carboxyl*-^{11}C]methionine), are described in the IUPAC document: http://goldbook.iupac.org/index.html.
In the case of "fluorobenzene" labelled with fluorine-18:
[^{18}F]fluorobenzene is correct;
[^{18}F]benzene is incorrect, since benzene does not contain a fluorine atom.
Likewise, for technetium-III, forming a 1:1 complex with DTPA:
[^{99m}Tc]TcDTPA^{2-} is correct, while [^{99m}Tc]DTPA^{2-} or ^{99m}Tc-DTPA^{2-} are incorrect, since the chelator itself does not contain a technetium atom.

According to these conventions, isotope symbols in square brackets in combination with nouns or verbs are meaningless and are to be avoided in a published chemical text or presentation. Instead, the element symbol together with the mass number must be used without any brackets. There is no contradiction or likelihood of confusion with the indication of a carrier-free state (see above), since nouns and verbs cannot be enriched or labelled with the indicated isotope.

Consequently, for example [^{11}C]compound, [^{125}I]-substitution, [^{18}F]-derivative and [^{68}Ga]conjugate, are incorrect terms, since these nouns are not names of "chemical compounds". These words should instead read as follows: ^{11}C-compound, ^{125}I-substitution, ^{18}F-derivative and ^{68}Ga-conjugate (note: with hyphen!), or preferably: ^{11}C-labelled compound, substitution with iodine-125, ^{18}F-tagged derivative, and ^{68}Ga-labelled conjugate. Analogously, ^{68}Ga-complex of a chelator, ^{111}In-chelate, ^{124}I-iodinated antibody, or ^{99m}Tc-labelled conjugate are to be used.

Equally, terms commonly found in literature such as [^{11}C]labelling, [^{64}Cu]-labelling, or [^{18}F]-(radio)fluorination are erroneous, because 'labelling' and 'radiofluorination' are verbs and nouns and of course do not contain "chemical elements". These expressions should instead read: ^{11}C-labelling, ^{64}Cu-labelling and ^{18}F-fluorination, while the prefix 'radio' is anyway redundant here.

When a radionuclide is mentioned in isolation (i.e. without a compound name or ouside of the context given in the previous paragraph), fluorine-18, technetium-99m, etc., should be used, rather than "^{18}F" and "^{99m}Tc" (at least not without definition) as this would, strictly speaking, infer a carrier-free status for the radionuclide (see above). Generally, terms such as 18F, F18, F-18, or 99mTc, Tc99m, Tc-99m must not be used. Correspondingly, "^{76}Br-" (the bromine-76 anion) is more accurately described in texts by the terms [^{76}Br]bromide ion or [^{76}Br]Br^{-}, and by analogy, [^{177}Lu]Lu^{3+} is correct for the description of the [^{177}Lu]lutetium cation rather than "^{177}Lu^{3+}".

N.B.: It is understood, however, that when used in chemical formulae or graphical reaction schemes, nuclide symbols or those of their ions are given without square brackets.

Compounds labelled with metallic radionuclides and their complexes follow of course the same conventions as given above for covalently labelled compounds, e.g., [^{223}Ra]$RaCl_2$, [^{99m}Tc]$NaTcO_4$, [^{99m}Tc]Tc-MDP, and [^{99m}Tc]Tc-MIBI. Examples of radiometal-labelled conjugates are: "[^{68}Ga]Ga-chelator-Z" (where "Z" is a place holder for a molecule to which the [metal(ligand)$_n$] complex is attached to, e.g., a peptide or antibody such as in [^{68}Ga]Ga-DOTA-TATE and [^{89}Zr]Zr-DFO-trastuzumab.

It should be mentioned that square brackets are of course also used to denote metal complexes, and care should be taken to avoid confusion (see also the above cited: Nomenclature of Inorganic Chemistry, IUPAC Recommendations 2005 (www.**iupac**.org/fileadmin/user_upload/databases/Red_Book_2005.pdf). Illustrative examples include [^{99m}Tc][$Tc(CO)_3(OH_2)_3$]$^+$, [^{111}In][In(DTPA)]$^{2-}$, [^{111}In][In(oxyquinoline)$_3$] ([^{111}In]In-oxine), or [^{64}Cu][Cu(ATSM)].

The terms '(radio)isotope' and '(radio)nuclide' are often used incorrectly in texts, e.g., erroneously inferring that "isotope" means "radioactive nuclide" or even "labelled compound".

N.B.: All (radio)isotopes are (radio)nuclides, while the reverse is not true!
For example, both the nuclear reactions ^{176}Yb(n,γ)^{177}Yb (induced by thermal neutrons) and ^{124}Xe(p,2n)^{123}Cs (induced by charged particles) produce radionuclides, but only the first one leads to a radioisotope of the starting material.

For the sake of clarification the definition of these terms are repeated below:
(N.B. These terms are (slightly different) defined in the IUPAC Gold Book)

- 'Nuclide' indicates an atom, characterised by its numbers of protons (atomic number, identifying its elemental nature) and of nucleons (indicating its mass). There are isobaric, isotonic, isodiapheric, and isotopic nuclides (see chart of the nuclides), which can be stable or radioactive, e.g., ^{1}H and ^{2}H are stable, ^{3}H is radioactive.
- 'Isotopes' are nuclides of the same element (same proton number, i.e., atomic number), but having different numbers of neutrons (hence different atomic mass). Isotopic nuclides of different energy state are called isomeric nuclides, isomeric isotopes or isomers, such as technetium-99g and -99m.
- 'Isobars' are nuclides with the same mass number, such as ruthenium-100, technetium-100, molybdenum-100, etc.
- 'Isotones' are nuclides with the same number of neutrons, but different numbers of protons, such as hydrogen-2 (deuterium) and helium-3, or lithium-8, beryllium-9, boron-10, carbon-11, nitrogen-12 and oxygen-13.
- 'Isodiapheres' are nuclides with the same difference of neutrons and protons, such as boron-10, carbon-12, nitrogen-14, oxygen-16, fluorine-18,

neon-20, etc. (difference: zero), or titanium-49, vanadium-51, chromium-53, manganese-55, iron-57, etc. (difference: five excess neutrons).

Radiochemical yield (RCY)

Prior to a discussion of radiochemical yields, two facts should be considered:

- Synthetic chemistry is the science of combining elements and molecules to form compounds in proportion to their components; i.e., in relation to their masses. Since it is the number of atoms/molecules that are generally referred to, amounts of materials are usually expressed in moles. (Example: 1 mole of carbon is combusted with 1 mole oxygen gas to form 1 mole of carbon dioxide; $C + O_2 \rightarrow CO_2$)
- Radiochemistry is the chemistry of radioactive materials (elements, atoms, molecules). With the exception of the field of 'hot-atom-chemistry', the standard laws and conventions of chemistry still apply, with the exception of accounting for radioactive decay.

The correction for the decay of two (or more) radioactive samples to an identical point in time enables the law of relative masses to be employed; i.e., the application of established chemistry concepts, definitions and terms.

'Radiochemical yield', calculated using decay-corrected radioactivity values for products and starting compounds, is identical to the concept of 'chemical yield'. Logically, the reference time for correction of decay must be identical for describing a particular reaction, irrespective of whether it is chosen to be the end of radionuclide production, the end of bombardment, the start of synthesis, the end of synthesis, or any convenient reference time point.

Definition of radiochemical yield (RCY)
Radiochemical yield is the amount of activity in the product expressed as the percentage (%) of starting activity used in the corresponding process (e.g., synthesis, separation etc.). The **quantity of both must be decay corrected to the same point in time** before the calculation is made. (see also Appendix)

It should be understood, that under this definition, the radiochemical yield is only related to the considered radionuclide, and it does not include compounds labelled with all radionuclides that may undergo the same reaction as the radionuclide of interest (e.g., Ge-68 in Ga-68 preparations).

N.B.: Sometimes the amount of radioactivity produced at the end of a nuclide production cannot be (or is not) determined, for example with gaseous compounds such as [^{11}C]CO. However, it is recommended to measure the radioactivity of resultant product or to determine the 'trapping efficiency' of the labelled starting material and use this to correct the RCY calculation.

If it is accepted that **radiochemical yields are always decay corrected** (as is general convention in the wider nuclear and radiochemistry fields), it makes 'newly created' terms to describe yields with radioactive materials superfluous,

enabling an approach that is consistent with mainstream chemistry nomenclature; and it simplifies the understanding of our scientific findings and concepts within and outside the field of radiochemistry.
Furthermore, it is good practise to report, if the radiochemical yield refers to an isolated or non-isolated product.

Consider the following example. "The (radio)synthesis of compound Y":
The first step of reaction of A and B formed compound C, which was converted into D, oxidised to E and finally hydrolysed to product Y that was isolated by preparative HPLC.

Description of chemical yields: The overall yield of product "Y" was 40 %. While the yield of C after the first step was 90 %, the yield of the conversion of C to D amounted only to 50 %; but the yield of oxidation and hydrolysis were almost quantitative.
Description of radiochemical yields: The radiochemical yield of product "Y" was 40 %. While the radiochemical yield of C after the first step was 90 %, the radiochemical yield of the conversion to D amounted only to 50 %; but the radiochemical yield of oxidation and hydrolysis were almost quantitative.

If it is understood that radiochemical yield is identical to chemical yield, the sentences are identical and easily comprehended. If non-decay corrected yields were used, the 'yields' would be totally different to the standard chemical description of yields.

By comparison, colloquial terms for "radio-yield" found in literature are neither necessary nor helpful: e.g., expressions such as 'radiochemical conversion', 'analytical radiochemical yield', 'radio-HPLC yield' must not be used as a surrogate for the accepted terms 'radiochemical yield' or 'radiochemical purity'. If these terms were to be used, the previous example would be even more nonsensical.

Also, a term such as 'radiochemical conversion' yield might give the impression that there is a nuclear change. Furthermore, other expressions such as 'radioincorporation', 'radio-oxidation', 'radiohydrolytic' yield etc. would have the same justification.
Equally, 'analytical radiochemical yield', 'radio-HPLC yield' should not be used as a surrogate for the accepted term radiochemical purity (RCP).

The following are examples of good practice when describing radiochemical yields:
'The radiochemical yield of "Y" was 67 % (based on HPLC analysis of the crude product)."
'The radiochemical yield* of "Y" was 67 %", with the following as a footnote:
"*determined by radio-HPLC analysis of the crude product", or
"*non-isolated, estimated by radio-HPLC,
or, in the general experimental section: "All radiochemical yields were determined by radio-HPLC analysis of the crude product, unless stated otherwise."
or alternatively use: 'The radiochemical purity of the crude product was 67 %.",

"The radiochemical yield of "Y" determined from an aliquot of the reaction solution amounted to 67 %."
or: "The radiochemical yield of crude "Y" was 67% based on the amount of activity eluted from the HPLC column".
Expressions such as 'conversion' or 'incorporation' may, however, be used in a semantic sense and even are indispensable in context of mechanistic discussions to avoid over-repetition of the same phrase in a text. For example: "The 'conversion' (or 'incorporation') proceeded with 50 % yield. Here it is clear from the context, that the radiochemical yield of the conversion or incorporation is intended. In this case, the prefix "radio" is to be avoided.

Definition of activity yield (AY)
Radioactivity yield is the amount of radioactive product expressed in Bq (MBq, GBq), which is obtained from a starting amount of radioactivity (e.g., produced from a cyclotron) and is **not corrected for decay**.
This term is useful, or necessary to indicate the amount of radioactive product obtained from a starting amount of radioactivity. If this is expressed as a "non-decay-corrected radiochemical yield" in %, it is significantly dependent on losses due to the technical manipulations used, and on their duration, in addition to the yield of the labelling reaction.
Thus, if a "radioactivity yield" is stated, e.g., to demonstrate the (economic) efficiency of a production process, the time required for all production steps should be carefully described in order to make results comparable! A rigorous scientific report/publication will indicate the length of reaction times used in addition to the time required for other technical manipulations. In this case, starting radioactivity levels can be calculated from reported radiochemical yields.

In an experimental section it should also state if a yield is estimated using the measured radioactivity of the isolated product, or if it was estimated, for example, by HPLC analysis of a sample of the crude product.
It is further recommended to specify how radioactivity, specific activity, etc. are analysed and measured; e. g., determined by HPLC. Although normally reported in the experimental section of publications, it may also be useful to include these clarifications in footnotes on slides and electronic presentations.

Definitions of purity

Chemical purity
Chemical purity is the absence of other chemical compounds/species.
(N.B.: 1. Chemically pure samples may contain isotopically labelled material!
2. Chemical purity is often erroneously described as ratio of the mass of carrier to the mass of other impurities. However, this is erroneous and would lead to a nonsensical result, i.e., that as the level of carrier decreases (and molar activity increases) the chemical purity would decrease! It is strongly discouraged, to report chemical purity in this manner.)

Radiochemical purity
Radiochemical purity is the absence of other radiochemical compounds/species.

(N.B.: Radiochemically pure samples may contain other non-radioactive chemicals.)

Radionuclidic purity
Radionuclidic purity is the absence of other radionuclides.

Radioisotopic purity
Radioisotopic purity is the absence of other radioisotopes. This refers to radioisotopes of the same element, but not to radionuclides of other elements!

N.B.: Here the 'property' of all these purities are defined. Generally in practice, the 'degree or extension of purity' is expressed in %, for example the 'radionuclidic purity' as the ratio, given as a percentage, of the activity of the radionuclide concerned to the total activity of the material; and so on.

Examples:

i) If there is a sample of acetyl-salicylic acid, labelled with carbon-11 in both carboxylic acid groups (acetyl- and benzoyl-position), this material is chemically, radionuclidically, and radioisotopically pure, but not radiochemically.

ii) Given, iodine-123 labelled para-iodo-bromo-benzene is chemically and radioisotopically pure (i.e., containing no other radioiodine isotopes), but it may accidentally also contain bromine-77. This compound would neither be radionuclidically nor radiochemically pure.

Physical units

Although it is not specifically the theme of these guidelines on nomenclature, attention must also be paid to the correct use of physical units, such as using the correct term for a given unit (see above molar activity for Bq/mole).

An example, often occurring in reports on nuclide production, is the incorrect use of "MBq/μAh" to represent the amount of radioactivity produced per μA beam current during a 1-hour irradiation, unless this is clearly stated. Actually, yield of activity means activity produced per current or per number of charged particles applied.
Thus, it is strongly encouraged to report either physical yields in units activity per charge (Becquerel per Coulomb, MBq/C) or saturation yields as activity per current (Becquerel per Ampere, MBq/μA), since everything else can be calculated from those parameters.

This issue has been under discussion for many years. In some instances 'measures' using other units may also be justified. If this is the case, however, definitions must be properly given. Such terms and their utility are explained on pp. 281-283 in the appendix of the IAEA-Tecdoc-1211 (2001): "Charged particle cross-section database for medical radioisotope production: diagnostic radioisotopes and monitor reactions". The topic was recently dealt with in great detail by Otuka and

Takacs in "Definitions of radioisotope thick target yields" (Radiochim. Acta **103**, 1-6 (2015)).

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Appendix

A) *Some Definitions from IUPAC Nomenclature Documents*

For completeness and comparison, several extracts of IUPAC Books are given:
The convention for naming radioactive matter is concisely described in 'Nomenclature of Inorganic Chemistry, IUPAC Recommendations 2005': (www.**iupac**.org/fileadmin/user_upload/databases/Red_Book_2005.pdf).
A more detailed treatment of these conventions are provided in chapter II-2 of 'Nomenclature of Inorganic Chemistry II, IUPAC Recommendations 2000' (Red Book II), and in the IUPAC Nomenclature of Organic Chemistry (Blue Book) prepared by Advanced Chemistry Development; found on the ACD website: http://acdlabs.com/iupac/nomenclature. The corresponding 'Compendium on Analytical Nomenclature' (Orange Book) is under revision. The version of 1998 is found under: http://media.iupac.org/publications/analytical_compendium/.
Additionally, a new draft IUPAC document on "Terminology on carrier, specific activity, and purities in nuclear and radio-chemistry, radioanalytical and radio-pharmaceutical chemistry" by Bonardi et al. (2014) is currently under discussion.

Indication of mass, charge and atomic number using indexes (Red Book)
The mass, charge and atomic number of a nuclide are indicated by means of three indexes (subscripts and superscripts) placed around the element symbol.
The positions are occupied as follows:

- *left upper index mass number*
- *left lower index atomic number*
- *right upper index charge*

A charge placed on an atom of symbol A is indicated as A^{n+} or A^{n-}, not as A^{+n} or A^{-n}.
For example: ${}^{32}_{16}S^{2+}$ represents a doubly ionized sulfur atom of atomic number 16 and mass number 32.

Hydrogen is an exception in that the three isotopes ${}^{1}H$, ${}^{2}H$ and ${}^{3}H$ can have the alternative names protium, deuterium and tritium, respectively, and the symbols D

and T may be used for deuterium and tritium. However, ^{2}H and ^{3}H are preferred, because D and T can disturb the alphabetical ordering in formulae. These names give rise to the names proton, deuteron, triton for the cations $^{1}H^{+}$, $^{2}H^{+}$ and $^{3}H^{+}$, respectively. Because the word 'proton' is often used in contradictory senses, i.e., for isotopically pure $^{1}H^{+}$ ions on the one hand, and for the naturally occurring undifferentiated isotope mixture on the other, it is recommended that the undifferentiated mixture be designated by the name hydron, derived from hydrogen.

It has to be pointed out here, that the lower-case characters p, d, t and the symbol α are also valid descriptors for the ions of hydrogen and helium, respectively, and are generally used when describing nuclear reactions, e.g., $^{14}N(p, \alpha)^{11}C$, or isotopically substituted solvents, such as DMSO-d_6 in NMR-spectroscopy.

Specifically and selectively labelled compounds (Red Book)
*An **isotopically substituted compound** has a composition such that all the molecules of the compound have only the indicated nuclide(s) at each designated position. The substituted nuclides are indicated by insertion of the mass numbers as left superscripts preceding the appropriate atom symbols in the normal formula.*

*An **isotopically labelled compound** may be considered formally as a mixture of an isotopically unmodified compound and one or more analogous isotopically substituted compounds.*
*An isotopically labelled compound is called a **specifically labelled** compound when a unique isotopically substituted compound is added formally to the analogous isotopically unmodified compound.*
*A **selectively labelled** compound may be considered as a mixture of specifically labelled compounds.*

Specific activity and molar activity (Orange Book proposal)
***Specific Activity**: 'The activity (A) of a specified radionuclide, or of a mixture of radioisotopes, in an amount of substance divided by the mass (m) of the total number of atoms present in it. Symbol: a = A/m.*
***Molar Activity**: 'For a specified isotope, the activity (A) of a molecule incorporating the radionuclide divided by its molecular weight (M) expressed in moles. Symbol: A_m = A/M.'*

Status of carrier (Orange Book proposal):
***Carrier-free**: 'A radioactive nuclide, which is <u>measurable</u> free from stable isotopes of the corresponding element.'*
***No-carrier-added: '**A preparation of radioactive nuclide which is <u>essentially</u> free from stable isotopes of the corresponding element.'*}

Radiochemical Yield (Gold Book and Orange Book proposal)
'The ratio of the activity of a specified radionuclide of a specified element after its radiochemical separation and its activity originally present in the substance undergoing the radiochemical separation.'

Radiochemical purity and radioactive purity (Orange Book proposal)

***Radiochemical purity**: 'Ratio of the activity of a radionuclide in a stated chemical species in a material over the total activity of all species containing that radionuclide in this material.'*
***Radioactive Purity**: 'Ratio of the activity of a stated radionuclide over the total activity of all radionuclides present in a material.'*

B) *Definitions and Units of Radiological Quantities*

Quantity	Definition	SI-Unit	Old Unit	Conversion Factor
Activity (Decay rate)	Number of radioactive disintegrations per time	Becquerel 1 Bq = 1 s^{-1}	Curie 1 Ci = 3.7 · 10^{10} s^{-1}	1 Ci = 3.7 · 10^{10} Bq 1 Bq = 2.7 · 10^{-11} Ci
Energy dose	Total absorbed radiation energy per mass	Gray 1 Gy = 1 J/kg	Rad 1 rad = 10^{-2} J/kg	1 rad = 10^{-2} Gy 1 Gy = 100 rad
Equivalent dose	Energy dose · quality factor of type of radiation	Sievert 1 Sv = 1 J/kg	Rem 1 rem = 10^{-2} J/kg	1 rem = 10^{-2} Sv 1 Sv = 100 rem
Ion dose	Electrical charge of ions produced in 1 kg air by radiation	Coulomb/kg	Röntgen R	1 R = 2.58 · 10^{-4} C/kg 1 C/kg = 3.876 · 10^{3} R

*SI Units = International System of Units