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80th Consultation on International Nonproprietary Names for Pharmaceutical Substances

Geneva, 18 – 21 March 2025

Executive Summary

Programme on International Nonproprietary Names (INN)

Access to Medicines and Health Products Division (MHP)
Health Product Policy and Standards Department (HPS)
World Health Organization, Geneva

80th Consultation on International Nonproprietary Names for Pharmaceutical Substances

Geneva, 18-21 March 2025 (hybrid face-to-face/virtual meeting)

EXECUTIVE SUMMARY

WELCOME and OPENING REMARKS

The 80th INN Consultation was opened by Dr Yukiko Nakatani, Assistant Director-General (ADG), Health Products Policy and Standards (HPS). Dr Nakatani expressed her gratitude to the INN Experts and advisors whose dedication and commitment ensures continued success of INN which remains a cornerstone of global public health. She noted that INN Experts have a substantial workload of new requests and that three key side meetings: the monoclonal antibodies, the cell and gene therapy, and the publications working groups, allow for more specialised discussion.

With the WHO facing huge financial challenges amid political tensions, the highly valued face-to-face format of INN Consultations may have to be curtailed and more use of virtual meetings may be necessary. However, the ADG recognised that the role of INN is more critical than ever and that it is a core WHO mandate, fundamental for patients' safety, equitable access to medicines, pharmacovigilance and regulatory harmonisation. Looking ahead, the ADG considered it essential to strengthen the link between INN and other nomenclature systems, especially Anatomical Therapeutic Chemical (ATC) classification. Additionally, raising global awareness of INN and its critical role in public health must remain a priority and the School of INN (SoINN) is an excellent initiative in this regard.

In closing, the ADG gave special thanks to the Expert Group, Special Advisors and the INN Secretariat for their hard work and wished them a productive meeting.

Dr Balocco, Unit Head, INN Programme and Classification of Medical Products, thanked Dr Nakatani for her words and echoed the hope to continue with face-to-face meetings.

ELECTION of CHAIR, VICE-CHAIRS and RAPPORTEUR

Prof Sarel Malan was nominated for Chair, Dr Akinola Adisa and Mr Adrian Evans were nominated to be Vice-Chairs of biologicals and chemicals respectively, and Dr Jim Robertson was nominated as Rapporteur; all nominations were agreed by the meeting.

NOTES of the 79th INN CONSULTATION

The Notes of the 79th INN Consultation were adopted without objection and the Chair thanked the Rapporteur for his clear and comprehensive report.

NOMENCLATURE of INN

During the 80th INN Consultation, 255 INN requests were discussed, including:

- 227 new INN requests, of which 147 were for biological substances
- 26 outstanding requests
- 2 objections

As a result of these discussions, 239 new names were selected, which are planned to be published in Lists 133 (one COVID-19-related request only) and 134 of proposed INN (p.INN). Six requests did not fulfil INN criteria (No INN), three were withdrawn by the applicant and seven requests were deferred for future discussion.

Four new stems/substems were selected, four suffixes were promoted to the pre-stem list and it was decided to review the description of three stems/suffixes before the 81st INN Consultation (*-fensine*, *-oxetine* and *-faxine*).

Open Database for Proteins (ODP)

The open database for proteins (ODP) now contains the sequence and structural features of 1,200 protein substances. Some inconsistencies remain and .doc files are missing for 150 substances.

The database can be accessed by INN Experts through IDMIS. It can be subjected to a BLAST analysis, and the extent of similarities and mismatches displayed. The database can also be accessed through the SoINN database by registered users but only has data for already published INN. Applicants and INN Experts should be encouraged to check the sequence of a new protein submission with that in the database to avoid unnecessary applications for identical proteins.

Cell Therapy Working Group

CAR-T cell therapy is a cancer therapy that involves the transduction of a patient's T lymphocytes with a chimeric antigen receptor (CAR). INN for CAR-T cells follow the standard 2-word cell therapy format, in which the infix *-cabta-* is used along with the -gene stem of the first word. A new CAR-T cell request involved the transduction of T cells with a messenger RNA (mRNA) encoding the CAR rather a viral vector. Where mRNA is used for the transduction, the working group proposed that the suffix of the first word should be *-rene* instead of *-gene* to highlight that a transient cytoplasmic mRNA is the carrier of the CAR coding sequence rather than a viral vector that persists in the nucleus, as this may impact the safety profile of the substance. The INN Expert Group agreed that an alternative suffix to *-gene* should be used and *-rene* was deemed acceptable by most. A few Experts felt that *-rene* was not sufficiently distinct from *-gene* but with no consensus on an alternative and with time pressing, the Chair requested that further suggestions be made via post-meeting comments[1].

The published definition for a tumour infiltrating lymphocyte (TIL) INN highlights the type of the tumour from which the TILs were derived. It was the opinion of the cell experts that patient-to-patient variability was greater than the origin of the tumour and that definitions could be broadened to include additional tumour types provided adequate supporting data on the spectrum of T lymphocytes from the alternative tumour was available. There was some concern though that this could result in unlimited requests for amendments of TIL definitions.

With the manufacturing process being a key aspect in defining a cell therapy substance the working group has revised the annex of the application form for cell therapies, requesting greater details and release criteria including potency assays, to adequately define the uniqueness of the cells.

Monoclonal Antibodies (mAbs) Working Group

Although there is a well-defined pathway of assessment of an INN request during which all aspects get checked and issues highlighted early in the process, some serious issues were uncovered recently quite late in the process. In one case, during preparation of a Proposed List it was noticed that a mAb INN had been assigned a *-bart* stem (artificial mAb) whereas it is unmodified and should have been assigned a *-tug* stem (unmodified mAb). Also, after publication, it was discovered that another mAb had the same sequence as a previously named mAb; after the applicant was informed, the request was withdrawn. In another case, the applicant of the recommended mAb INN *cixutumumab* (126)(88) informed the Secretariat that it had the same sequence as the previously named mAb *dacetuzumab* (98)(60) and to date both INN remain.

[1] In post-meeting comments, it was decided to defer further discussion on a *-rene* suffix to the 81st INN Consultation.

The new ODP database can help avoid such mistakes and applicants should be requested to use the database to ensure the sequence of their protein is unique and does not match a previous INN. However, the sequence of some early named mAbs was not provided and the Secretariat is requesting such missing information from applicants. Also, a more automated way of describing mAbs is being put in place by the group that should make the work of the Secretariat and the Experts easier.

INN and Adzynma

Adzynma is a recombinant purified bivariant enzyme that was authorised in the EU in Aug 2024 and the meeting were made aware that the Recommended INN had not been used by the EMA in the product's SPC and product label. It was known that Adzynma contains two sequence variants, Q23 and R23 (referring to amino acids at position 23) and had previously applied for an INN for each variant, with *apadamtase alfa* and *cinaxadamtase alfa* being assigned accordingly. The two variants co-exist in the active substance in a variable ratio from batch to batch, and with the company claiming no detectable difference in any measurable parameter, including bio-activity, between the two, the mixture was authorised by the EU Commission. The issue for the INN Group is that the EU SPC for Adzynma does not mention either INN, contrary to normal regulatory practice. Instead, the active substance is described as rADAMTS13, a company code, alongside the assigned ATC code (B01AD13) which is for the mixture of the two variants.

It was agreed that the INN Secretariat would write to the EMA to ask for an explanation as to why the INN have not been used, as per normal regulatory practice.

Publication Working Group

The publication working group comprises 21 experts with sub-groups assigned to chemicals, mAbs, non-mAb proteins, cell and gene therapies, and combinations of the above. There are also experts dedicated to translation from English into French and Spanish, in the preparation of Action & Use statements, and proof-reading. In preparing newly assigned INN for publication, the working group members have to respect strict timelines.

The group is currently working on obtaining chemical structures in electronic format rather than pictorial format, as many of them are complex and not easy to represent. Also, for short single strand oligonucleotides, two conventions are available; one is an IUPAC format and one comprises a single letter format, and the group decided to adopt the latter as being easier, clear and more recognisable. For radiolabelled components, two styles of specifying the isotope have been used in the past, and going forward one specific format will be used.

Nomenclature for metal containing substances should take into account valence charges, and small molecule complexes should be presented in a neutral state; however, for antibody drug conjugates containing metals, this is less important as proteins have many ways of ensuring neutrality.

An online tool is also being developed for use by the group to compare, search and view closely related structures.

Finally, Action & Use (A&U) statements are created by the Mode of Action (MoA) working group and are published in Proposed INN Lists to provide information on a single activity of the substance or its main intended use but are not published in Recommended INN Lists. A 2014 working document to harmonise the preferred expressions for stems, substems and prestems, is being updated by appropriate experts.

The group is currently working on Proposed List 133.

INN Stems and Pharmacovigilance

Time and knowledge of toxicity are two important aspects to pharmacovigilance (PV) and it is important to detect toxicity of a new medicine as early as possible. During clinical assessment of a

new drug, if the rate of adverse drug reactions (ADRs) is quite low, an ADR may not show up if only a limited number of patients have received it. A study of ADRs in USA from 1969-2002 revealed a wide range of time intervals between a drug being on the market to withdrawal because of serious ADRs, from a few months to, in one case, >20 years. In the case of thalidomide, it was first marketed in late 1957 but not withdrawn until late 1961, by which time many unfortunate cases of phocomelia had occurred.

ADRs are difficult to identify and diagnose because they mimic many other signs and symptoms. There are different methods to assess ADRs with spontaneous reporting being the most common. When a physician treating patients suspects and reports an ADR, such data can be collected and analysed by, for example, the Uppsala Monitoring Centre (UMC), with the main objective being to identify clusters of previously unknown but suspected ADRs. Some researchers group suspected ADR cases according to ATC codes at levels 2 or 3. However, within a given level 2-3 there can be many alternative medicines with different modes of action. Can INN stems help strength detection of an ADR?

Both EudraVigilance and VigiAccess are publicly available databases that can be searched for potential ADRs by product or by substance. Would there be value in searching such databases by INN stem? Using the VigiAcess database to study ADRs associated with two or more stem-related drugs, a profile of ADRs associated with a particular INN stem can be created. If a new drug with this particular stem is marketed, its ADR profile can be compared with the typical ADR profile for active ingredients with the same stem. Any clear discrepancy within the profile of the new drug would alert users to a possible new serious ADR. Such use of stems could be a useful adjunct in searching for new ADRs and can provide certain advantages.

A paper highlighting the use of stems in PV is under development.

INN Stem vs ATC Codes

Using JavaScript-based graphics, the INN Programme's IT manager demonstrated a simple colourful graphic way of how ATC codes and INN stems interconnect at the 5th ATC level. It allows a straightforward assessment of INN that do not have an ATC code and will assist in publication of INN; however, the reverse, determining substances with an ATC code but no INN is a bit more complicated. Problems can arise though when there are two ATC codes for the same substance and there needs to be a way to harmonise and check ATCs. Collaboration with the Oslo ATC Centre on this would be valuable.

Assigning Pre-ATC Codes to New INN

These reflections were shared for information and were not intended to be a solid proposal.

INN are generally assigned during early stages of clinical development when the level of knowledge of the drug substance is limited. In contrast, it is usually not until a drug is approved and marketed that an ATC code gets assigned (at the 5th level).

INN stems kick in at the 4th ATC level. For example, the 4th level N06AB, for selective serotonin reuptake inhibitors, contains 8 entries including *-oxetine*, *-traline* and *-peridone* stems. However, substances with the *-oxetine* stem are not limited to this 4th level group and 8 current *-oxetine* substances appear in three distinct 4th level groups: urologicals (G04B), antidepressants (N06A) and psychostimulants (N06B).

Could a pre-ATC be assigned to a drug under development with a new INN but not yet marketed and no ATC code assigned? In theory, the 4th level code N06AB for selective serotonin reuptake inhibitors could be pre-assigned to new drugs with the *-oxetine* stem. However, *ampreloxetine* is being developed for neurogenic orthostatic hypotension, whilst *esreboxetine* was under development for

neuropathic pain but no longer is, while assessment of it for fibromyalgia has restarted. So, assigning a pre-ATC would be difficult but would help strengthen the link between INN and ATC.

There could be disadvantages: a pre-ATC code could become obsolete and require amendment, or it could create confusion, or cause problems with regulatory agencies. However, the advantages would be to help identify gaps in research and preserve the historical development pathway. Might drug developers benefit from being assigned a pre-ATC code, suggesting action on a specific organ or condition, before evidence from clinical trials is available, and what might happen if the substance has a novel mode of action not yet created in the ATC tree? There are already many loose ends in ATC classification but a 'pre-ATC' concept could be adopted as part of the ATC assigning tasks. For such a venture, strong collaboration between INN and ATC experts would be necessary.

INN for Faecal Transplants

Faecal Microbiota Transplantation (FMT) is a therapeutic intervention involving the transfer of donated stool from a healthy donor to a recipient to restore microbial community structure and function in the recipient's gastrointestinal tract. Stool is collected from healthy donors, with only about 1 in 100 being found suitable following donor screening. After collection, stools are homogenised and mixed with saline, and introduced into the patient's bowel typically by rectal enema or colonoscopy, or via oral capsules. FMT comprises a complex, undefined mixture of microorganisms (primarily bacteria, but also archaea, fungi, viruses, and bacteriophages), their metabolites, and other biological components that collectively constitute the donor's intestinal microbiota. They are used primarily to treat *C. difficile* infections, with some good evidence for an efficacious effect, but are having increasing application in IBD and other metabolic disorders.

FMT are poorly standardised, containing thousands of microbial species, with high donor variability, unknown active components, and processing variability. There is minimal assessment of the constituents and measurement of functionality but as they pose a risk of infectious disease transmission, there is comprehensive donor screening.

There is a wide spectrum of live microbial therapeutics, ranging from FMTs to defined microbial consortia (specific bacterial strains in defined ratios), to single strain probiotics, with a variety of therapeutic targets and intervention therapies.

There have been a few requests for an INN for live microbial therapeutics, but no INN have been assigned due to high variability between donors, the absence of knowledge of which components provide the therapeutic effect and the mode of action of any effect. It was noted that a previous request for an INN for a single strain of lactobacillus was turned down as the MoA was not clear. It does however have an ATC code at level 3, and there is a request pending to assign an ATC at level 5

An INN for Colchicine?

Colchicine is a plant-derived therapeutic substance that has been used for several centuries to treat gout. It acts partly by inhibiting activation and migration of neutrophils to sites of inflammation and partly by direct anti-inflammatory effects. The plant and its medical use were first described in the medical literature in the 1800's and currently the British National Formulary notes its use in treating acute gout and familial Mediterranean fever.

The IUPAC name of colchicine is N-[(7S)-1,2,3,10-Tetramethoxy-9-oxo-5,6,7,9-tetrahydrobenzo[a]heptalen-7-yl]acetamide. It is listed on ATC and also has a JAN and USAN, but no INN. Two related substances have INN, *demecolcine* (colchamine) and *thiocolchicoside*; however, Pubmed hits on these compounds are mainly for colchicine, and the two substances with INN appear not to be useful clinically or not even used. Other plant-derived medicines have been assigned INNs, but there are also several that have not.

It was proposed that colchicine be assigned an INN.

Generally, INN are not selected for herbal preparations nor for medical substances whose use antedates the INN Programme; this does not preclude making a recommendation, as an INN can be published without a formal request.

SCHOOL OF INN (SoINN)

The 23rd SoINN Steering Committee (SC) meeting was held on Monday, 17 March 2025 with two parts: one open to pilot sites and the other restricted to SC members.

There are currently six pilot sites: Ramon Lull University in Barcelona, the University of the Western Cape in Cape Town, the University of Grenoble, France, the University of Alcalá in Madrid, the University of Monastir in Tunisia, and the UPO University in Italy. Since these pilot sites are run by academics, it is not surprising that most of their activity is devoted to developing pharmacology courses based on INN and their stems, particularly the 'Stems in Pills'.

A new publication, the second edition of the course 'Learning Pharmacology with the Use of Stems', was highlighted.

Two universities had their students develop posters for the general public: the University of Grenoble in France and the International University for Science and Technology in Syria. This latter university is being proposed to be a new SoINN pilot site. The use of INN was also promoted at various conferences and meetings. Also noted was the start of two new research projects, one in linguistics as part of a master's degree, and another that could lead to a doctoral thesis.

Two new pilot sites are currently being considered: one in Sao Paulo, Brazil, which works primarily in the field of pharmacovigilance, and the other at Fundan, University in China. This latter site works on an important project: the translation of the SoINN website into Chinese. These sites allow the SoINN to gain a foothold in South America and Asia.

To increase the visibility of the SoINN, it now has articles on Wikipedia in its English, French, Catalan and Spanish versions, and a SoINN presence on LinkedIn will be created.

Establishing a coherent classification of drugs is one of the major challenges of clinical pharmacology. In current classifications, the criteria used can be quite disparate, for example, some drugs are grouped according to their clinical activity (e.g. antiepileptics), some according to their pharmacological effects (e.g. anti-inflammatories), others according to their mechanism of action (e.g. beta blockers), and still others according to their chemical structure (e.g. tricyclic antidepressants). The definition of INN stems does not escape this heterogeneity of criteria. The ATC classification is based on anatomic, therapeutic, and chemical and pharmacological data. The SoINN ambition is to harmonize INN stem and ATC classifications, both of which are developed under the aegis of WHO. This ambitious project has been entrusted to a working group that includes two German academics, and indeed, in Germany, teaching is based on a classification adopted by all universities and which is based solely on mechanisms of action.

The courses on the SoINN website remain relevant while the course on INN chemical aspects is very large and will be split into two parts. The Stem in a Pill section continues to grow steadily and now has more than twenty chapters which are to be compiled into an e-book.

Finally, the list of medications developed by the Spanish Ministry of Health is no longer based on the names of specialties but on INN.

COLLABORATORS' UPDATES

Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

The European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA) have recently published a joint European regulatory network strategy up until 2028. This strategy aims to ensure

that the European regulatory network has the necessary resources to ensure that, among other things, the European Union is competitive in the development and manufacture of medicines. It has an integrative, One Health approach, which recognises that human and animal health and the environment are closely interrelated.

The European Commission's Critical Medicines Alliance published a report recently that recommends priority actions to strengthen the supply of medicines in the EU and prevent shortages. Alongside this, the EMA is setting up the ESMP (European Shortages Monitoring Platform) as part of its extended mandate, to gather information about medicine availability, supply and demand. Also, the EU list of critical medicines has been published by the EMA, in collaboration with EU member states and stakeholders, as part of efforts to prevent shortages and safeguard public health. It comprises active substances deemed essential for healthcare systems across the EU/EEA, prioritising their continuous supply to prevent shortages that could significantly harm patients and challenge health systems.

The AEMPS has exceeded the average score of European agencies in HMA's benchmarking programme and the work carried out by the Agency to adapt to the new European regulation on veterinary medicinal products was also highlighted.

In 2024, the AEMPS celebrated its 25th anniversary as the state agency attached to the Ministry of Health responsible for guaranteeing society, from a public service perspective, the quality, safety, efficacy and correct information on medicines of human and veterinary use and medical devices.

In general discussion, it was further explained that from February 2025, EU marketing authorization holders are now obliged to submit details of medicinal products that might have supply problems and one such detail is the name of the active substance, which is of relevance to the INN Group.

It was also highlighted that the FDA's G-SRS is a public database whereas IDMP is a commercial standard run by ISO, and the Uppsala Monitoring Centre is overhauling its database to align with IDMP. Through all this there is a need to protect the WHO's INN, and this is being addressed with IDMP referencing the INN. It was further suggested that where there are differences in understanding what constitutes the active substance, it would be useful at the next Consultation, to address these points and explain further the work of the IDMP. This was taken onboard by the Secretariat.

Brazilian Pharmaceutical Substances Nomenclature Committee (CTT DCB)

Since the last INN meeting, two important improvements have occurred relating to pharmaceutical substance nomenclature in Brazil.

First, Resolution Anvisa nº 955/2024*, consolidates 12 years of separate rules and creates a fast procedure to approve names by shortening hierarchical procedures. It is accompanied by Normative Instruction IN 342/2024, under which new names will be published; this preserves the authority of the CTT DCB committee, but no longer requires the approval of the Agency's director. Guide 76/2025 was also approved, which contains procedures to update the list of common names and contains explanations about the understandings that lead to approval of names, with examples. This is an important improvement because examples were not possible in the previous text.

*https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2025/dcb-publicado-o-novo-marco-regulatorio

Second, the coordinator of the CTT DCB committee is helping in setting up the School of INN (SoINN) in Brazil with two events organised, an internal meeting with specialists, and an external seminar. A collaboration with the SoINN-Brazil team has been approved by the Brazilian Pharmacopeia in its Working Plan for 2025. Also, in June 2025, the SoINN-Brazil representatives will meet with the Brazilian Committee of Pharmaceutical Substances Nomenclature (CTT DCB) along with the Brazilian Pharmacopeia's coordinator. Finally, SoINN–Brazil representatives have been

invited to present a seminar at the Brazilian Academy of Pharmaceutical Sciences (ACFB), at its Educational Program** on June 23, 2025.

**https://cienciasfarmaceuticas.org.br/eventos/

European Medicines Agency (EMA)

An update was given on the 'Human Medicines Highlights 2024' which provides a high-level overview of recommendations for new marketing authorisations (Human medicines in 2024). In 2024, 114 medicines received a positive recommendation from the CHMP for marketing authorisation of which 46 contained an active substance new to the EU, including:

- Beqvez (*fidanacogene elaparvovec*), a gene therapy treatment for haemophilia B that delivers a human coagulation FIX gene via an adeno-associated virus (AAV) vector.
- Ixchiq (chikungunya vaccine (live, attenuated)), the first EU vaccine to protect adults against disease caused by Chikungunya virus.
- Two new influenza H5N1 vaccines, both containing the same active ingredient but with different indications, one for zoonotic infection (Celldemic) and one for pandemic preparedness (Incellipan).
- mResvia is the first mRNA vaccine for protecting against lower respiratory tract disease caused by respiratory syncytial virus (RSV), for use in adults aged 60 years and older; the mRNA encodes the membrane-anchored RSV-A glycoprotein F.

COVID-19 vaccines

- Kostaive (*zapomeran*), a self-amplifying messenger RNA (sa-mRNA) that encodes the surface glycoprotein of SARS-CoV-2, the virus that causes COVID-19; it also encodes a replicase that amplifies additional copies of the mRNA intracellularly.
- Three approved vaccines (Comirnaty, Spikevax and Nuvaxovid) were adapted to the Omicron JN.1 variant, one (Cominarty) to the KP.2 subvariant, and one (Bimervax) to the Omicron XBB.1.16 subvariant.

Neurology

- Leqembi (*lecanemab*) for the treatment of mild cognitive impairment or mild dementia due to Alzheimer's disease in patients who have only one or no copy of ApoE4, a specific form of the gene for apolipoprotein E.
- Qalsody (*tofersen*) a new therapy for the treatment of adult patients with amyotrophic lateral sclerosis (ALS) who have a mutation in the superoxide dismutase 1 (SOD1) gene.

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) assesses the safety of products and highlights of its monthly meetings are published online. An overview of important new safety advice issued in 2024 is also included in the Human Medicines Highlights 2024.

Instituto de Salud Pública de Chile (ISP)

The Institute of Public Health (ISP) is the regulatory authority for medicines and other health products in Chile. It has several technical and scientific departments including Occupational Health, Environmental Health, Medical Devices, the Biomedical Department, and the National Medicines Agency. ISP is also the reference laboratory for environmental health, clinical laboratories and medicines. Among many other activities, it performs confirmatory HIV testing and histocompatibility testing for transplants, performs viral and bacterial sequencing, and implements diagnostic tests that it transfers to the country's clinical laboratories.

ISP is one of the eight medicines regulatory authorities in the Americas that has obtained recognition as a reference medicines authority from the Pan American Health Organization (PAHO). It is currently working to renew this recognition to become one of the authorities listed by the WHO. The evaluation

of authorities is carried out using the Global Benchmarking Tool (GBT) which consists of indicators that assess the performance of authorities in fulfilling eight functions: drug registration, pharmacovigilance, market surveillance, licensing of establishments, regulatory inspections, supervision of clinical studies, laboratory testing, and release of vaccine batches.

One of the ISP activities this year will be the meeting of the WHO Advisory Group for Drug Statistics Methodology, which will be held in April 2025. The ISP will also have a new version of the Scientific Conference, which is held every two years.

Currently, one of the greatest challenges in drug control is illegal trade and more efforts are being focused on that. This has been reinforced with the creation of a surveillance department. The ISP is seeking and developing IT tools to help in this task; for example, a system developed at Swissmedic for rapid data capture for surveillance is being assessed by the Institute.

Together with other drug regulatory authorities in the region (including Colombia, Cuba and Mexico), the ISP is promoting the creation of a community agency that will allow it to optimize its resources and make its processes more efficient.

https://www.who.int/initiatives/who-listed-authority-reg-authorities

Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Since the previous INN Consultation, the JAN Expert Committee met on two occasions and 9 names have been published, including one biosimilar.

Supplement 2 to the 18th edition of the Japanese Pharmacopoeia was implemented in June 2024 and its English version was published in December 2024. These can be downloaded freely on the Japanese government website. Furthermore, the Pharmacopoeial Discussion Group (PDG), which brings together the European Pharmacopoeia (Ph.Eur.), the Indian Pharmacopeia Commission, the Japanese Pharmacopoeia (JP) and the United States Pharmacopeia (USP), with the World Health Organization (WHO) as an observer, held an interim videoconference on 6 March 2025. The next face-to-face PDG meeting will be hosted by the JP in Tokyo this October.

Lastly, on 7 January 2025 the PMDA renewed its corporate logo on the occasion of the 20th anniversary of its establishment. The PMDA has established its Purpose, in order to cope flexibly with the constantly changing environment surrounding pharmaceuticals, medical devices and regenerative medicines. As the first initiative of its 20th anniversary, its Purpose was made with the hope to "endeavor for our continuous progress and create a world where each and every one can feel peaceful and can lead vibrant and healthy lives, together with all stakeholders". As a second initiative at its 20th anniversary, PMDA's new logo representing the PMDA's Purpose was decided by vote of all PMDA's members. The new logo aims to ensure that each and every member of the PMDA staff works with the Purpose in his/her mind, and that it continues to create "Tomorrow's Normal" together with everyone around the world.

https://www.pmda.go.jp/english/about-pmda/0022.html

The PMDA comment on living in a peaceful world was well taken and supported by the meeting.

Also in discussion, the PMDA confirmed that for biosimilars it continues to add a code on to the end of the JAN. In contrast, the recommendation made to the WHO by the Expert Group to implement the Biological Qualifier (BQ) has never been implemented by the WHO with the result that different arrangements have been made around the world to identify biosimilars. It was then agreed that the Expert Group should write to WHO for clarification on its stance of the BQ; a letter will be drafted and circulated for comment.

Therapeutic Goods Administration (TGA), Australia

In October 2024, the TGA made the decision not to register *lecanemab* (LEQEMBI) on the Australian Register of Therapeutic Goods (ARTG) for the treatment of patients with Mild Cognitive Impairment (MCI) due to Alzheimer's disease and Mild Alzheimer's dementia (early Alzheimer's disease). The decision has now been confirmed following reconsideration sought by the sponsor.

From 2021 the government and the TGA introduced a raft of legislations to control importation, supply and access to vaping products in Australia. The overall intent is to protect the health and wellbeing of Australians and ensure that the gains made on smoking cessation are not reversed due to uptake of vaping.

As a result of these new laws, since 1 July 2024, Australian enforcement officers have been inspecting retail stores across the country to undertake education and compliance activities relating to the unlawful supply, commercial possession and advertising of vaping goods. Over 7 million vaping products have been seized by the Australian Border Force and the TGA since 1 January 2024. From 1 July 2024 to 31 December 2024, the TGA has issued 54 infringement notices to businesses and individuals for the alleged advertising, supply, possession or import of unlawful vapes. More information is available on TGA's vaping hub.

Vaping hub | Therapeutic Goods Administration (TGA)

United States Adopted Names (USAN)

The 2024 winter USAN Council meeting took place on December 5-6, in Las Vegas, Nevada. Names for 30 drug substances were reviewed and discussed. Ten new stems (-alkib, -cractin, -deg, -grel, -guran, -iprone, -melnant, -nosine, -padin, -tifator) and 5 new infixes (-raf-, -serti-, -tra-, -luta-, -bru(ti)-) were approved and added to USAN's stem list.

Meeting topics discussed included: a negotiations update, USAN website metrics, Bifunctional Protein naming (PROTAC), the October 2024 INN Consultation, and ISMP and FDA's medical error reports. A USP update and a discussion on Artificial Intelligence in drug naming also took place.

Twenty-one INN applications for proposed USAN were prepared and forwarded to the INN Programme to be discussed at the 80th INN Consultation.

From October 2024 through March 2025, USAN staff have processed, researched, and made recommendations for approximately 130 USAN applications and forwarded this information to the USAN Council for their review and name selection. Through March 2025, 75 USANs will have been adopted for 2025. Revenue from 3 other applications was also realized. Currently, there are approximately 150 active USAN negotiations.

The 2025 Summer meeting of the USAN Council is scheduled for June 12-13, 2025, in Washington, D.C., hosted by the American Pharmacists Association (APhA).

Uppsala Monitoring Centre (UMC)

The Uppsala centre continues its work on the global implementation of ISO IDMP. Within that, it has seen a need from different global organisations for greater standardisation of vaccines, as per the presentation in the Open Session adjoining this Consultation. The Centre appreciates that INN has named some modern vaccines and recognises that more classical vaccines are not within the scope of INN, but given the expertise within the INN group, input on the more classical ones from the INN Experts on conformity and standardisation was requested as this would be a great help.

Also, the UMC has now implemented an INN flag within its global dictionary which will make it simpler to note which substances have an INN and which ones do not.

World Customs Organisation (WCO)

An update on activities of the international customs community with respect to the Harmonized System classification of INN pharmaceutical substances was provided.

Since the October 2024 INN Consultation, the 40th Scientific Sub-Committee (SSC) of the WCO, which convened in January 2025, examined, *inter alia*, the Harmonized System (HS) classification of INN Proposed Lists 130 and 131. It agreed on all but two substances, *efdoralprin alfa* (INN) and *efsudenermin alfa* (INN), which will be discussed at the next session of the SSC.

The SSC further reviewed the classification of all INN with the stems '*-golix'* and '*-relix'* and ensured that all of them have been classified in the HS in a consistent manner. It also examined the classification of *pegmispotide* (INN), which was pending from the previous session.

It also discussed and concluded the possible amendment to the Explanatory Note to the heading of 'antibiotics' (29.41), aiming at clarifying the difference between antibiotics and antibacterials.

The 75th Harmonized System Committee has adopted the classifications agreed by the SSC as well as the amendment to the Explanatory Note to the antibiotics heading.

The WCO is looking forward to discussing the classification of new INN substances submitted by the WHO to the future sessions of the SSC and expressed its appreciation for the continued and invaluable technical advice that Dr Lasseur of the INN Secretariat provides to the WCO examinations in relation to INN.

World Intellectual Property Organisation (WIPO)

The WIPO joined others in congratulating the INN Programme on its hard work and dedication. WIPO also announced that the latest notified list of INN had been shared with WIPO Member States and the data had been integrated into the global brands database.

CLOSE of MEETING

The Chair thanked all his colleagues around the table and online for participating, and for their support and efforts to attend the meeting. The Chair also thanked those who helped in preparing the meeting and everyone for the open way of discussing often difficult issues.

Dr Balocco thanked the Chair for his leadership of the group.

Next meeting

The 81st INN Consultation will be held in Geneva on 14-17 October 2025.

OPEN SESSION for INN STAKEHOLDERS

80th Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances

WHO HQ, Geneva, 18 March 2025

The Open Session held in conjunction with the 80th INN Consultation was opened by Dr Balocco, Unit Head, INN Programme and Classification of Medical Products, who welcomed all to the meeting. She expressed her gratitude to stakeholders for bringing their expertise and their views to the INN Experts to have robust discussion. She reminded participants that the Open Session is open to stakeholders only and not for external dissemination as some presentations may be confidential and not to be shared outside.

The meeting was chaired by Professor Sarel Malan, who expressed his pleasure in learning from stakeholders, adding that whatever gets presented will be taken further for discussion at the plenary session of the 80th INN Consultation.

BioOra

BioOra, a New Zealand (NZ) company, presented details of their anti-CD19 CAR-T cell therapy product for treatment of B-Cell Non-Hodgkin Lymphomas and which incorporated the unique feature of a Toll-like receptor 2 (TLR-2) co-stimulatory domain. Their product targets an urgent unmet clinical need, as there is no alternative access to CAR T-cells in New Zealand. It is manufactured by a proprietary automated protocol developed to increase manufacturing feasibility, improve consistency and reduce vein-to-vein time. Phase 1 and 2 data show a favourable safety profile with reduced cytokine production *in vitro*, a significantly lower rate of Cytokine Release Syndrome (CRS) and Immune effector Cell-Associated Neurotoxicity Syndrome (ICANS) in clinical practice compared to second generation CAR-T products.

Manufacturing has started and clinical approval in NZ was obtained in 2018 with phase 1 beginning a year later running through to 2023. Phase 2 assessment began in 2024 and is on-going, with 2026 being the target for submission of a new medical application and 2027 for standard of care delivery in NZ. While getting an INN is not a requirement for NZ for medical applications, the company felt it important to achieve this to facilitate licensure and market entry.

In the absence of feedback from WHO regarding their application, the company made representation at this Open Session in response to a suggestion from the Secretariat, although it was clarified that it is not unusual for applicants not to hear from WHO until a month after the Consultation at which the application is fully assessed by the INN Experts. The company was also interested in how the process works.

ASBM

This was the ASBM's 25th appearance before the INN Expert Group to advocate for distinct biologic nomenclature and international harmonization, and to provide support for the Biologics Qualifier (BQ), an important programme to assure safety of biologics and biosimilars. Much had happened since the last meeting including the withdrawal of the USA from WHO, but ASBM remains committed to supporting the work of the INN and the BQ, which was developed over 10 years ago but not yet implemented. The benefits of nomenclature remain clear: proper product identification and avoiding inappropriate substitution, better pharmacovigilance (PV), proper attribution of AEs and most importantly increased accountability of manufacturers for their products. Post marketing surveillance and accurate PV are especially critical for biosimilars; yet as biosimilars proliferate, many different but highly similar products continue to share a non-proprietary name. Also, now that there is a decreased emphasis on clinical data for approval of biosimilars, PV programmes and distinct

naming become more important. An international naming system would also benefit the use of biosimilars globally, including in less developed countries which may not have good PV systems.

The ASBM recognises that the BQ as recommended by the Expert Group has not been withdrawn and assumed remains supported by the Group. Over the past 10 years, ASBM has been engaged with regulators from Canada, USA, Australia and Japan to evaluate the BQ and several of them initially gave support. However, delays in moving the BQ forward have resulted in supporters adopting their own schemes, such as the 4-letter suffix adopted in the USA, or the simple suffix adopted by Japan. Many, however, have expressed willingness to harmonise if WHO implements the BQ. There has also been consistent support for the BQ amongst prescribers and physicians.

The ASBM announced it will work to confirm continued support of the BQ among past and present supporters. It will also conduct outreach activities focused on three key groups – physicians, patient groups and regulators, and expects to find continued broad support for a voluntary distinct nomenclature standard. Whatever data is accrued from these three groups will be shared at the 81st INN Consultation in October.

The Chair expressed his gratitude to the ASBM for the time and effort put into its support of the BQ.

In discussion, it was clarified that the BQ proposal addressed biologicals and not specifically biosimilars, with biosimilarity being a regulatory approach. It was also stated by the INN Secretariat that it is unclear why WHO management has left the BQ in limbo and suggested that the Expert Group, if it so desires, could request the Secretariat to look further into this to bring it to a conclusion. The INN Secretariat also expressed its gratitude to the ASBM for attending every meeting with data and suggestions and expressing support for the BQ.

Naming of vaccine antigens according to ISO 11238

The ISO Identification of Medicinal Products (IDMP) is a standard for the unique identification and exchange of medicinal products and comprises a suite of five ISO standards. ISO 11238 in particular focuses on substance identification, with vaccine antigens currently being addressed by substance experts in ISO from, amongst others, EU regulatory agencies, FDA, Uppsala Monitoring Centre (UMC) and industry. In order to achieve a broad consensus, the group is currently reaching out to other interested parties. The speaker (a biotech assessor at the Dutch Medicines Evaluation Board Agency [MEB] and the Chair of the Substance Validation Group of the Heads of Medicines Agencies [HMA]) addressed this Open Session to describe the work being done and to request input in this activity from the INN Expert Group.

Developing substance identification for chemicals is relatively straightforward; however, biologicals are more challenging. INN are available for most biologicals but not for most vaccine antigens which generally have pharmacopeia names that are descriptive and not precise. The intention now is to capture all details, in a structured hierarchal way, of an antigen for both human and veterinary vaccines to accurately identify each vaccine. This approach is not to replace INN, but to create a common language for vaccines where there is no INN and for which the need became apparent during COVID-19. INN will be the preferred names where available, e.g. many mRNA vaccines have INN, but traditional vaccines are not assigned INN and this is where most effort is being applied.

The current approach being taken to describe vaccine antigens in detail involves a hierarchical system of structural features with greater detail shown at successive levels. For example, a hepatitis A virus inactivated vaccine would have the descriptive lines: hepatitis virus A, whole; hepatitis virus A, Strain CR326F, whole; hepatitis virus A, Strain CR326F whole, inactivated; hepatitis virus A, Strain CR326F whole, inactivated by formaldehyde; with each line sequentially providing more detail of the antigen. A similar approach was shown for a fusion protein antigen, antigens forming vesicles, a live chimeric virus and conjugated vaccines. In each case, a building block approach is being used to provide a specific definition of the antigen. Other types of antigens would include viral vectors and

genetically engineered viruses and bacteria. In finishing, the speaker called upon the INN Experts to provide input using their extensive background of expertise on naming medicinal substances, including complex biologicals.

In discussion, it was highlighted that INN are only assigned when a formal application is made and that they get applied to labels, whilst the definitions that accompany a name are much more scientific. The Chair noted that having opened lines of communication, this should continue through the Secretariat so that the INN Group as a whole can contribute.

Close of session

The Chair thanked all who presented for the interesting exchanges, and closed the session.