INN Working Doc. 23.577
January 2024
Distr.: PUBLIC
ENGLISH ONLY

77th Consultation on International Nonproprietary Names for Pharmaceutical Substances

Geneva, 17-20 October 2023 (hybrid face-to-face/virtual meeting)

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

EXECUTIVE SUMMARY

WELCOME and OPENING REMARKS

Dr Clive Ondari, Director, Health Products Policy and Standards (HPS) and Director of the INN Programme, was honoured to open the 77th INN Consultation. He extended a warm welcome to the experts, advisors and representatives of intergovernmental organizations and was grateful to all who had contributed their expertise, time, and energy to make this consultation possible. He was pleased that many had travelled to Geneva and hoped that with time, all participants would be here face-to-face. He took a moment to emphasise to both long serving and new comers, the WHO code of conduct, that Experts must work independently and not for their home organisation, to do so impartially and confidentially according to WHO rules, and to do so to the best of their ability and in a timely manner.

Dr Ondari informed participants that this year the INN Programme celebrated its 70th year and that INN had been crucial in ensuring the safe and standard use of pharmaceuticals worldwide. He took a moment to reflect on progress and how it continued during this 77th Consultation and which shows the depth and breadth of responsibilities that WHO extends to the Experts. At this meeting, he noted there were 252 requests to address, another record-breaking number, with 217 new requests encompassing 146 biologicals and 71 chemicals, which shows the ever-evolving landscape of pharmaceutical innovation and in particular in the field of biological medicinal substances. There were also 32 outstanding requests that necessitate rigorous examination and resolution. In addition, there were 6 COVID-19 related requests plus 2 Variants of Interest vaccine requests, which reflects the work carried out by the Experts, and senior WHO administration has expressed its gratitude for the work achieved amid the COVID-19 response.

Revision of cell therapies nomenclature shows dedication in refining INN schemes, and he also noted the growth of INN activities such as the School of INN. The nomenclature for COVID-19 VOC and VOIs was to be discussed which is of immense global importance. The Open Protein Database (OPD) for published INN proteins is a pioneering project that will simplify data access for stakeholders as well as the Secretariat and Experts. Dr Ondari further highlighted that WHO had been in discussions examining its potential role in the global implementation of the Identification of Medicinal Products (IDMP) ISO standard and that there was general support to appoint the WHO Collaborating Center for International Drug Monitoring, Uppsala Monitoring Centre (UMC) as the maintenance organization for the Pharmaceutical Product Identifier (PhPID). WHO is also exploring ways of making use of its expertise on INN and existing infrastructure in supporting the work related to Global Substance Identification (GSID) and the IDMP standards. The INN Programme would be kept updated.

He finished his introductory remarks by thanking the entire INN Secretariat team for working diligently in preparing for the meeting.

Professor Malan thanked Dr Ondari for his kind words and his support of the INN Group, and noted that his term at WHO was coming to end. Dr Ondari acknowledged that he had spent 25 years in various roles at WHO, mostly at WHO HQ but also in Nairobi. He felt that the leadership of the INN Team was in very good hands and wished them all the best.

Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products replied that it had been an extreme privilege to work with Dr Ondari who had always been wonderfully polite, kind and helpful.

ELECTION of CHAIR, VICE-CHAIRS and RAPPORTEUR

Professor Sarel Malan was proposed as Chair of the meeting, and this was agreed by all. Mr Adrian Evans and Professor Menico Rizzi were proposed as vice-chairs for chemicals and biologicals respectively, and this was agreed. Dr Jim Robertson was proposed as Rapporteur and this was agreed.

WELCOME by CHAIR

The Chair had recently spent 6 months with the INN Programme at WHO HQ and expressed his admiration at the amount of work achieved by the INN Secretariat between meetings. He also expressed his gratitude for the support he received whilst on sabbatical in Geneva. He welcomed all participants and thanked them for the comments submitted prior to the meeting, and with many new participants, he called for a tour-de-table.

NOTES of the 76th INN CONSULTATION

The Notes of the 76th INN Consultation were adopted without objection and the Chair thanked the Rapporteur for his clear and comprehensive report.

NOMENCLATURE of INN

During the 77th INN Consultation, 252 INN requests were discussed, including:

- 217 new INN requests, of which 146 were for biological substances
- 32 outstanding requests
- 3 objections

As a result of these discussions, 245 new names were selected, which are planned to be published in Lists 130 (COVID-19-related requests only) and 131 of proposed INN (p.INN). One request did not fulfil INN criteria (No INN), 6 had been withdrawn by the applicants and 6 requests were deferred for future discussion.

Six new stems/substems were selected, six suffixes were promoted to the pre-stem list and it was decided to review the descriptions of two stems.

INN Amendment Requests

Following the discovery of an error in the structural definition of an INN there was debate about how or if an amendment could be performed. Where the error is made by the INN Programme, a change will be published, but when a change is due to an error by the applicant in its original data submission, then it is highly unlikely that a simple amendment could be made. For example, when a substance no longer aligns with its given Definition, there are safety implications and essentially a new INN should be sought. The USAN also agreed that a new USAN would be appropriate in such circumstances. Applicants needed to be aware that during clinical development of a substance, changes however subtle can impact on the validity of an already assigned INN.

COVID-19 Vaccine Active Substances against variants of SARS CoV-2

In April 2021, in response to the rapid development of COVID-19 vaccines, the INN developed Working Document 21.520 on ‘International Nonproprietary Names for Variant

COVID-19 Vaccine Active Substances'. This announced that the assignment of INN for vaccines against SARS CoV-2 Variants of Concern (VOC) would be expedited and that the usual fee would be waived. However, since March 2023 there have been no further VOCs, and only Variants Under Monitoring (VUM) and Variants of Interest (VOI) have been described. Also, in May 2023, the WHO announced that COVID-19 was now an 'established and ongoing health issue' which no longer constituted a Public Health Emergency of International Concern (PHEIC). Consequently, it was proposed by the Secretariat that 21.520 needed to be re-assessed with regard the timelines for assigning INN to COVID-19 vaccines, especially for VUMs and VOIs, and also to re-consider the waiving of the fee now that vaccine manufacturers were making profits from them. The INN Programme should remain flexible though, especially in the event of the appearance of a VOC and there may be a need for expedited assignment of INN for seasonal vaccines such as for influenza and updates of COVID-19 vaccines.

It was mooted that the approach to the naming of variant COVID-19 vaccines should also be re-assessed. The evolution of the virus is not following a perfectly linear path and variants are appearing more on the tips of branches of a tree rather than exactly on the main trunk, and so relating the INN of one variant to a previous one perhaps is no longer appropriate. One other aspect of 21.520 that requires attention was the applicability of the naming process to protein COVID-19 vaccines. Viral vector, plasmid and mRNA vaccines all have regions of the active substance that remain constant amongst a manufacturer's vaccines. However, this is not the case for protein vaccines and in line with any other protein biological substance, each protein should have its own distinct INN beyond any common stem. It was also highlighted that for any wording in documents, it is the active substance of a vaccine that is named and not the 'vaccine'.

The timelines for assigning an INN were clarified. The procedure operates within a legal framework approved by the World Health Assembly, and INN adopted at this Consultation would become Proposed INN by June 2024. This time period includes time for post-meeting comments and the mandatory 4 months period for objections. However, where an application for an INN for a vaccine needs to be expedited, the time for post meeting-comments could be reduced and by accelerating the work of publication experts, a Proposed INN for a name assigned at this Consultation could be ready by January 2024, saving 6 months. Regulators present at the meeting however felt that even with such a reduced timeline for seasonal vaccines, influenza vaccine manufacturers who are now developing mRNA vaccines would have difficulty in using INN in labelling and would likely stay with the common names used to date.

It was agreed by the Experts that with the pandemic downgraded from a PHEIC, it was no longer necessary to have a special COVID-19 procedure. For this Consultation however, the current process would apply but that a new procedure needed to be developed which included pandemic health emergency situations, an accelerated procedure for certain COVID-19 related substances whilst non-emergency vaccine substances would follow the standard INN assignment procedure.

Harmonisation of -*motide* and -IMUT for immunomodulatory polypeptides

The INN Programme names peptides that are 'immunological agents for active immunization' with the stem -*motide*; in contrast USAN names immunomodulatory peptides

with the stem -IMUT. Attempts to harmonise these two systems have been underway for some time.

In January 2023, the INN Secretariat sent its most recent proposals for harmonisation to CBER, FDA. In April, CBER responded that it could not align fully with these INN proposals, especially for mixtures of peptides. The INN Secretariat sent further points for consideration to CBER in May and awaits a response. Discrepancies in harmonisation remain.

The FDA representative present at this Consultation noted that he would try to contact those at CBER responsible for peptides to push forward the discussion.

WHO INN Open Database for Proteins (ODP)

A programming expert had been employed within the INN Team to develop a database for INN proteins, to be named the INN Open Database for Proteins (ODP). The objective was that data within the ODP would be easily accessible, searchable, and can be updated by both the INN Experts and the INN Team. The primary goal was to create a structured database that consolidates information currently scattered across various file formats such as .doc, .pdf, and others. The database is being designed to offer a user-friendly browsing experience, support advanced searching capabilities, and allow users to update, edit, and correct information within it. This will aid INN Experts with new requests by giving them easy access to all relevant information on protein substances already assigned INN, along with the capacity to perform multi-sequence alignment using well-established tools like BLAST (The Basic Local Alignment Search Tool). The INN Team will update the database with newly registered INN substances and generally provide assistance to the Experts.

Software extraction tools for migrating and structuring the INN data currently stored in MedNet to the ODP have been developed and 70% of 889 protein substances have already been migrated and validated; 18% require further editing while 12% of data are missing. The BLAST tool will display a summary of the level of sequence comparison and a detailed side-by-side display showing precise amino acid comparisons. Currently, the INN data stored in MedNet is in various file formats resulting in inefficient data retrieval and time wasting. Dr Balocco expressed her gratitude to those involved in this development. The project had been presented to the ECBS, who were very supportive, and hopefully the INN Experts would be also.

Dr Balocco added that she attends IDMP/GSID group meetings but unfortunately there had been no agreement within the group on a common identification standard. However, if a substance has an INN, the INN Programme can provide a GSID, which in essence could be a qualifier for all substances, including biologicals. Ultimately, the conclusions from the IDMP group will be presented to the WHO Executive Board which will feedback to the INN Programme, but it had to be noted that ISO standards do not belong to WHO.

Nomenclature of Gene and Cell Therapy Substances

A small working group of cell and gene therapy INN Experts have been re-considering the nomenclature scheme for gene therapy, cell-based gene therapy and cell therapy substances as the current schemes result in overly long and complex INN. The current schemes involve two-word names for gene and cell-based therapies, with both words having random prefixes

plus infixes for the type of gene, vector or cell. Cell therapy substances have one-word names. The proposals tabled by the working group can be summarised as follows:

- Remove the random prefix from the second word (vector component or cell component)
- Keep the random prefix of the first word as short as possible without diminishing uniqueness
- Keep gene infixes as short as possible e.g. one syllable, taking pronounceability into consideration
- Shorten existing gene and vector infixes to one syllable
- Autologous cell based-gene therapies will retain the *auto-* prefix
- Allogeneic cell based-gene therapies will continue with no prefix
- Some landmark two-syllable gene infixes e.g. -cabta- could be retained.
- The cell infix *-adstro-* (adipose mesenchymal stem cells [MSC]) should be discontinued and *-stro-* should be used for all MSCs.

According to these proposals, for example, the gene therapy substance *onasemnogene abeparvovec*, would be shortened to *onasemgene parvec*, whilst the cell substance *betibeglogene autotemcel* would be shortened to *betiblogene autotemcel*. If the cell was allogeneic, the second word would simply be *temcel*; that is, there would be no prefix and the absence of *auto-* indicates that it is an allogeneic cell. If the cells were genetically engineered, the current prefix/infix ged- would be shortened to ge-, as in getemcel for allogeneic substances or autogetemcel for autologous substances. *In discussion*, for plasmid-based gene therapies, the second word 'plasmid' with no random prefix was felt to be too technical and an alternative term '*plasvec'* was mooted. It was further queried if the second 'vector' word could be dropped altogether; however, the nature of the vector can impact side effects and it was deemed important to retain this in the name. Similarly, gene editing can change the nature of the cell and it is important to maintain *ge-* in the name with the fine details of the editing in the Definition. The use of the prefix *allo-* for allogeneic cells was discussed but ultimately dismissed in favour maintaining the current status of no prefix for allogeneic cell substances. Some concern was expressed that by minimising the length of the random prefix of the first word for gene therapy and cell-based gene therapy substances, distinct names could run out rather quickly; this would have to be addressed as and when it occurred, but may be alleviated by the myriad of gene infixes that get used in the first word. Some concern was also expressed that by dropping the prefix from the second word of gene therapy substances, that with time the word may get dropped altogether. Overall, though, the proposals were well received.

Historically a one-word name for these substances had been proposed but for simplification, two words were adopted with a random prefix on both words. This new proposal represents a small backwards step but was needed to simplify these INN. There was also argument that the second word even without a prefix is worthwhile to maintain as new vectors get developed.

The Chair sought approval from the INN Expert Group of these recommendations for gene and cell therapy nomenclature and this was given. These recommendations would be shared with CBER and USAN to reach agreement on a harmonised system and if accepted by them will be applied going forward.

The Chair thanked the working group for their recommendations which moves this particular scheme in the right direction.

INN over the years

The Chair, Professor Malan, described a project he had undertaken on how INN had progressed since their inception 70 years ago. During the lifetime of the Programme, he described how there had been a steady number of pharmaceutical substances named but that in the last decade numbers had increased significantly, with a total of 11453 INN having been assigned through 2022. Analysis of trends by stem classification show that overall, from a peak in the 1960's, the major therapeutic groups of CNS drugs, anti-infectives, antiparasitics and cardiovascular drugs substances had steadily declined (with the exception of antivirals) and that the huge growth in INN over the past decade had been due mainly to anti-neoplastic and immunomodulatory drugs. The anti-neoplastic drugs were primarily monoclonal antibodies and the tyrosine kinase group of inhibitors (*-tinib*). There is a similar but less marked trend for INN being marketed as approved medicines with only about 1 in 4 named drugs achieving marketing approval.

He commented on the WHO's Essential Medicines List (EML) that outlines the minimum medicine requirements for a country's basic health-care system. Interestingly, only about 3.9 % of all substances that get an INN end up on the EML. Most substances on the EML have been around for a long time as newer drugs do not necessarily have a new mode of action although may be more effective. For example, the newest therapeutic CNS drug added was in 2003. On the other hand, many new-anti-infectives, especially anti-virals, have been added onto the List.

In compiling this data, Professor Malan highlighted that he had received considerable help from members of the INN Secretariat.

School of INN (SoINN)

The Chair of the SoINN Steering Committee (SC) reported that since the last meeting of the SC, progress had been made thanks to the meeting held in May in Grenoble with five University pilot sites: Grenoble (France), University of the Western Cape (South Africa), Alcala (Spain), Monastir (Tunisia) and Ramon Lull (Spain). There had been two days of intense discussion which enabled the launch of more than 30 projects.

The meeting began with a presentation by Professor Siefert, Hannover Medical School, on his pharmacological classification of drugs based on mechanism of action. This is similar to the WHO ATC classification and the INN stem-based system, and there was an agreement to work together to develop a convergence between these three main classifications.

It was also reported that the SoINN has two publications in progress: a short letter to the Lancet highlighting that in the past 5 years 90% of new INN incorporate a stem, and a proposal to the New England Journal of Medicine for an article on the evolution of research in the various pharmacological classes on the basis of new INN.

Most of the meeting was devoted to monitoring the projects decided in Grenoble including two new courses in preparation, one on antibiotics the other on regulatory aspects in the field of medicine. Research projects include INN and pharmacovigilance, INN and medication errors, linguistic aspects of INNs and INN and artificial intelligence. Educational projects have been set up for improved teaching of pharmacology and the website continues to grow

with the development of FAQ's. The development of the use of INN in Morocco and Syria in progress.

The Chair of the SoINN SC stressed that the SoINN is not a closed group and anyone and everyone was invited to participate.

Advertising SoINN subgroup

Work is in progress to set up a subgroup of the SoINN to promote its presence. Currently the group is very small and volunteers were requested from a diverse background to take part in such a subgroup, either from the INN Expert Group or other interested colleagues. The group would meet monthly by teleconference, to identify stakeholders and key congresses where the SoINN could be promoted, and to target various bodies such as universities, professional societies and scientific journals possibly via interactive communities such as LinkedIn, Twitter and YouTube, with the overall objective of making the INN more visible to the world. Dates have been set for the forthcoming monthly meetings and outcomes will be discussed at the next SoINN steering group meeting and reported to the next INN Consultation.
Chair thanks those involved in the SoINN and noted the excellent progress it was making.

COLLABORATORS' UPDATES

Brazilian Pharmaceutical Substances Nomenclature Committee (CTT DCB)

Since the last INN Consultation (in March 2023), the Brazilian Committee for Nomenclature of Pharmaceutical Substances (CTT DCB), a committee of the Brazilian Pharmacopeia, had held five meetings (in April, May, June, Aug and Sept), in which 41 pharmaceutical substance names, including four excipients and one medicinal plant, were approved. All of them were linked directly to a medicine registration process in ANVISA, the Brazilian Medicines Agency.

European Directorate for the Quality of Medicines & HealthCare (EDQM)

The meeting heard that earlier this month, the Pharmacopoeial Discussion Group (PDG), which previously consisted of the European, Japanese and US Pharmacopoeias, with the WHO (International Pharmacopoeia) as observer, had welcomed a new member, the Indian Pharmacopoeia Commission. The PDG harmonisation process is always a long and complicated process, but is important in order to move towards global harmonisation and interchangeability of common analytical methods and excipients that are described in the pharmacopoeias, so this was a welcome development.

In addition, Ph. Eur. Supplement 11.4 was published at the beginning of October 2023. Two of the monographs that were revised were *Water for injections* and *Purified water*, which now specifically permit the use of the relatively new test for quantifying endotoxins using recombinant factor C as an alternative to the classic limulus amoebocyte lysate-based methods. Recombinant factor C is a synthetic reagent, while the lysate in the classic endotoxin test is derived from species of the horseshoe crab, including two species that are endangered in parts of the world. This is another step towards alleviating the need for these animal resources.

During the development of a Ph. Eur. monograph, an INN definition for a peptide substance was identified that appeared to be incorrect. It had been discovered by the original manufacturers that one of the amino-acid residues was in the D configuration, and not L as

originally thought. The incorrect structure was also provided in the original patent; this patent was subsequently corrected, several years later, with a certificate of correction appended to the patent. Apparently, no-one thought to inform the INN Secretariat about this change. The corrected structure is indicated in the CAS record and other sources online, while other sources refer to the original (incorrect) structure, often while citing the CAS number alongside. This is an example of one of the difficulties that the INN Secretariat faces, where there is a lack of communication from manufacturers and/or authorities regarding changes that take place, sometimes many years after the product first enters the market. The EDQM will contact the INN Secretariat with further details of the corrected structure.

European Medicines Agency

The EMA representative informed the meeting of concerns expressed by some vaccine manufacturers to the EMA regarding the timelines of INN assignment. These were mainly for mRNA-based vaccines against influenza, both seasonal and pandemic, and second generation COVID-19 vaccines. In one case, a company reported to EMA that its experience for variant updates of COVID-19 vaccines showed that an immediate start of the accelerated INN procedure could not be assumed and a resulting extended procedure meant that the approved INN could only be used post marketing approval. However, the EMA has always stated that if there is an INN then it should be used. Vaccine manufacturers also felt that INN restrictions to changes of a vaccine substance could be a hurdle during development as the sequence (of an mRNA vaccine) needed to be locked in place for the INN. It was also noted that when changes are not related directly to a new COVID-19 variant of concern (i.e. part of the coding region), then the procedure would not be accelerated. Another issue raised by developers was if multi-valent mRNA vaccines could be considered as a single substance. Finally, it had also been expressed to EMA that developers of prophylactic mRNA vaccines would like a clear separation in the INN from therapeutic products. These are all questions manufacturers have been asking, and which they may discuss with the INN Programme.

The EMA representative noted that some of these issues matched discussions that had already taken place at this Consultation and a mechanism by which the EMA could interact more with specific applications would be useful, especially as the EMA is not aware if a company applies for an INN and if INN requests are pending or approved, and relies on companies being transparent.

The Chair acknowledged the need for better communication, possibly with a list of questions from EMA for the Secretariat and vice versa, along with more regular meetings to discuss these issues.

Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Since the previous INN Consultation, the Japanese Approved Names (JAN) Expert committee met four times following which 36 names have been published, including three COVID-19 related substances and three biosimilars.

Supplement 1 to the Japanese Pharmacopoeia (JP) 18th edition was implemented in December 2022 and its English version was published in June 2023*. Currently, Supplement 2 of the 18th JP is being prepared which will be implemented in June 2024.

* https://www.mhlw.go.jp/content/11120000/001111831.pdf

Therapeutic Goods Administration (TGA), Australia

It was reported that the TGA has a new Head & Deputy Secretary, Professor Tony Lawler, who is a specialist emergency medicine physician and commenced working at the TGA in June 2023.

Dr Raffaella Balocco, INN Team leader, visited the TGA on 27 September 2023 and over 600 people attended her agency-wide presentation either in person or virtually, which demonstrated how much attendees valued the work of the INN. Attendees were from the TGA, Commonwealth Health Department, IP Australia and Australian Pesticide and Veterinary Medicines Authority (APVMA). The session had been opened and moderated by the new Head of TGA, Professor Tony Lawler and also in attendance was the Chief Medical Adviser as well as a number of Division and Branch Heads. An informal question-and-answers session with stakeholders was held in the afternoon that provided a more relaxed setting for learning about INN. It was attended by 18 people from the TGA, the Health Department, IP Australia and the Australia Commission for Medicine Safety. The TGA representative thanked Dr Balocco for taking time out of her busy schedule to visit the TGA. It had created a formal commitment between INN and not just TGA but other Australian health institutions.

From 1 September 2023, printed Product Information (PI) inserts are no longer required in the packaging of injectable medicines administered by health professionals in Australia. This change only affects injectable products administered by health professionals, including nurses, pharmacists and doctors. However, injectable products used by patients or their carers will still have a copy of the PI.

Dr Balocco thanked the TGA for her excellent reception.

United States Adopted Names (USAN)

The 2023 summer USAN Council meeting took place on June 9, 2023, with four members of the Council present and one participating virtually. Fifteen other participants took part in the meeting. Names for 34 drug substances were reviewed and discussed. Ten new stems and infixes were approved and added to USAN's stem list. One stem definition was revised. Meeting topics discussed included a Negotiations Update, USAN website metrics, the March 2022 INN Consultation, ISMP and FDA's medical error reports and a COVID-19 drug substances update.

From April to September 2023, USAN staff have processed, researched, and made recommendations for approximately 127 USAN applications and forwarded this information to the USAN Council for their review and name selection. Through September 2023, 182 USAN have been adopted for 2023 and currently, there are approximately 190 active USAN negotiations.

Twenty-eight INN applications for proposed USAN were prepared and forwarded to the INN Programme to be discussed at the 77th INN Consultation.

The 2023 Winter meeting of the USAN Council is scheduled for December 7-8, 2023.

United States Food and Drug Administration (FDA)

With regard to nomenclature, the FDA representative had no new FDA issues to report but commented that the FDA do not name prophylactic vaccines using USAN or INN, and vaccines assigned INN at this Consultation would be named in-house by CBER using a common name.

He highlighted that he had been attending the INN Consultations for almost 20 years as the FDA-USAN liaison council officer, but with his second 10-year term coming to an end he would be retiring imminently. Two individuals, both chemists with pharmaceutical backgrounds, are being appointed to replace him at the FDA, one of whom would attend INN Consultations in the future; potentially though he would attend the March 2024 Consultation.

United States Pharmacopoeia (USP)

The meeting was reminded that USP is >200 years old and as it is not being part of government, it has to find its own financial resources which it achieves by selling physical reference standards. A new successful project is the supply of physical samples of impurities; these are not formal standards but compounds that are mentioned in monographs. The USP is procuring them, synthesising them and qualifying them. The project is called pharmaceutical analytical impurities and its catalogue is growing.

It was further highlighted that handling all the compounds mentioned in the USP would be impossible without a good database and the USP made the decision to use the Global Substance Registration System (G-SRS) as its central repository of chemical information. It is an open-source software created in collaboration between US Food and Drug Administration (FDA) and National Center for Advancing Translational Sciences (NCATS) with USP participation. It is free and consistent with the ISO 11238 standard. The chemical information on 200,000 compounds can be readily downloaded. The European Medicines Agency (EMA) is also a big supporter of G-SRS.

In discussion, it was noted that no single system is being followed by all organisations. The meeting was reminded that in his opening remarks Dr Ondari had highlighted that WHO was involved in discussions on global implementation of the Identification of Medicinal Products (IDMP) ISO standard. The INN is meeting regularly with FDA and other collaborating centres on this and ultimately a project will be presented to the Executive Board and, if adopted, governance of any database will be given to the safety group at WHO.

World Customs Organisation (WCO)

The WCO representative provided an update of activities of the International Customs Community with respect INN. The Scientific Sub-Committee (SSC) of the WCO convenes every January and the forthcoming SSC meeting will examine, among others, INN Proposed Lists 128 and 129. It will also examine further the classification of three substances of p.List 126, that the Harmonised System (HS) Committee could not agree on during its previous meeting (these are *imlunestrant*, *sirpefenicol* and *efrilacedase alfa*). All other INN had already been classified by the HS Committee.

The WCO expressed its appreciation of the excellent contribution of Dr Lasseur of the INN Secretariat who has provided valuable technical advice to the Scientific Sub-Committee during the examination of the HS classification of INN. The WCO representative further

congratulated the INN Group on its fruitful meeting and thanked it for its hard and meticulous work on these significant matters.

WHO Collaborating Centre for Drug Statistic Methodology

In January 2023, the Centre published the ATC/DDD Index plus Guidelines for ATC classification and DDD assignment, in both Spanish and English. The main tasks of the Centre are to assign new ATC codes and establish DDDs for drugs with ATC codes. Consequently, about 120 new ATC 5th level codes were assigned in 2023, and about one third of these were in ATC first level, L, for antineoplastic and immunomodulating agents. Most of these applications derived from Europe and USA. The Centre also established 34 new DDDs and undertook 38 ATC code alterations, 90% of which were due to a change at L04A *Immunosuppressants* for which six new ATC 4th levels have been established. Following a public consultation, it was decided to base these new 4th levels upon pharmacology only.

An ATC/DDD educational course was held in Portugal in April 2023 and the annual international ATC/DDD course was held in Oslo in June. The Centre was also involved in a European Pharmaceutical Market Research Association (EphMRA)/WHO harmonisation meeting in March, and a WHO Academy course for which the Centre reviewed modules related to ATC/DDD methodology. In addition, the Centre is developing an application programming interface to make it easier for users to implement new ATC and DDD codes. Finally, the Centre is also working with ATCvet codes with the last annual meeting of the working group held in November 2022 and the next one in November 2023. About 100 new 5th level ATCvet codes were included in the ATCvet index 2023.

World Intellectual Property Organization (WIPO)

The WIPO representative provided a follow-up on the WIPO/WHO Memorandum of Understanding on Information Exchange on INN. Since the previous Consultation in March, WIPO had published on its Global Brands Database (GBD), Proposed Lists No. 129 Regular Edition, COVID-19 Special Edition and Addendum.

It was also reported that its GBD Webpage, where the INN are published, had received 224 million page-views in the last 6 months, which is about half of the total page-views for the WIPO website and represents an important exposure for these datasets.

The representative expressed interest in the School of INN Advertising sub-group and would appreciate more information about cooperative activities.

CLOSE of MEETING

The Chair thanked all participants for their commitment, their comments, and for the very good debates from which everyone learns, and looked forward to seeing everyone in March (at the 78th INN Consultation).

Dr Balocco thanked the Chair and vice chairs for their excellent chairing of the meeting. The outstanding work of the INN Secretariat, especially all that goes on behind the scenes, was similarly acknowledged.

Next Meeting

The 78th INN Consultation will be held in Geneva on 19-22 March 2024.

OPEN SESSION for INN STAKEHOLDERS

77th Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances

(a hybrid meeting with some participating virtually and some present at WHO HQ, Geneva)

Geneva, 17th October 2023

All participants of the 77th INN Consultation stakeholders Open Session were welcomed by Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products. Dr Balocco reminded everyone that although the meeting is referred to as an Open Session, all matters discussed should be kept confidential and not disclosed to anyone outside of the meeting.

The floor was given to Professor Sarel Malan to chair the meeting. He similarly welcomed all, and was pleased to see those around the table who had travelled to Geneva. He invited the first stakeholder to make their presentation.

MaaT Pharma

MaaT Pharma is a French company developing biological compounds aimed at restoring diversity in the microbiome to enhance the survival of cancer patients. The products are manufactured from faecal material with the first generation deriving directly from humans, and second-generation substances being co-cultured faecal material. The company's lead asset, MaaT013, in enema form, is in phase 3 studies for acute Graft-versus-host disease whilst an oral capsule format will enter phase 2b studies this year. There are issues of viability with the native faecal product and a lyophilised co-culture donor-independent platform using a synthetic oral microbiome capsule is in non-clinical development.

In anticipation of regulatory challenges of their product, including INN designation, the company had requested comment from the INN Programme on the requirement for INN for these substances. Human microbiota contain trillions of microorganisms including bacteria, archaea, phage and viruses, and with difficult analytical methods, it was the opinion of the company that these complex products would not require INN. There are several microbiome products currently on the market, ranging from single to a consortium of microorganisms, through to more complex entities containing single or pooled faecal donations, or co-cultivated cultures. To date, no INN has been assigned to these products and the company was interested in discussing alternative nomenclature for them with the Experts. Some potential prefixes/suffixes for these substances were presented such as *MiConsor* for a consortium of microorganisms (along with species names), *CoProPool* for complex pooled donor products, and *CoProCo* for complex cultivated products.

Discussion focused on the extent to which the biome substance could be defined. The company's products are less diverse than the human biome, and so are easier to decipher with identification of different strains and micro-organisms. In addition, manufacture will be comparable to the banking system of biotech systems, with no variability between batches. Batches will be quite small and will have different profiles for different indications, e.g. for

solid tumours, with specific batches prepared accordingly and used for the specified indication. However, even for products deriving from the same donor, there will be day-to-day variation. The proportion of different microorganisms, their family and genera can be determined but it would be almost impossible to be fully precise as to what is present.

Dr Balocco added that one such substance had been discussed in the past and that what is important is to be able to define what is named. If the substance cannot be defined, then no INN can be assigned, but if it can, then an INN can be provided. The Chair added that the INN Experts were not able to provide a decision at this point and what would be required is a formal application so that the data describing the substance to be named can be assessed properly.

The company noted that they would appreciate participating on this subject in the future, and would be glad to provide data.

ASBM

The ASBM has supported the INN Group's Biological Qualifier (BQ) scheme since its inception in 2012, and since then has doggedly presented data on the importance of a BQ to enhancing patient safety and pharmacovigilance (PV). However, they have also learned that WHO moves slowly, has many global health issues to deal with and has many stakeholders. Almost 10 years after the inception of the BQ, with no further action ensuing, a WHO report in 2021 highlighted that a lack of consistency in naming biosimilars had caused concern in prescribing, prescription mix-ups, unintended switching and traceability, and concluded that naming and labelling was important for product identification, PV and prescribing.

When the BQ was first proposed, ASBM noted that several global regulatory agencies supported the scheme, including the US FDA which eventually adopted its own not dissimilar system comprising a random four-letter suffix. Other supporting agencies await the WHO implementing a global system. In the EU, the EMA has stated that it does not need a BQ as it has an alternative system in place but recognises the value of a unified system. Several arguments have been raised by stakeholders opposed to a BQ; however, in each case these have proven to be unfounded. For example, it had been stated that distinguishable names may imply inferior products, but this has not been the case in USA. In addition, surveys have shown that a supposed lack of support by physicians and global regulators was incorrect.

Over the years, the WHO has attempted to evaluate the BQ: a provisional implementation of the programme was suggested in 2016, and in 2017 a pilot BQ project was discussed. In 2018, the project was put on hold for data gathering. The ASBM would be interested in knowing the exact the status of these approaches. Over these years also, the ASBM has surveyed and met with many global regulators and physicians and the vast majority support distinct nomenclature. The lack of action with the BQ has forced many regulators, either assigning the same non-proprietary name to biosimilars or in some cases to adopt their own system. However, most of them are willing to support a WHO system if it is implemented.

The ASBM made a proposal to quantify support for the BQ. By the next INN Consultation in the spring of 2024, the ASBM announced that it would reach out to national regulatory authorities and health ministries globally for formal support for distinct naming, and share the results with the INN at its Spring INN Consultation. It acknowledged support for a BQ system and with the debate having continued for 10 years now it strongly encourage the WHO to take a leadership role.

Dr Balocco noted that the department had a new ADG and that WHO was soon to have a new Director-General. The WHO has been asked to work on a Global Substance Identifier (GSID) and there may be an opportunity to bring in the BQ as part of this. The INN Programme is in fact ready to implement a BQ. Dr Balocco expressed hope that a decision would be taken soon as the INN by itself is not sufficient for PV.

The Chair thanked the ASBM for the work that has gone into this and for persevering with it.

The Chair thanked all presenters and discussants and closed the meeting.