

**73rd Consultation on  
International Nonproprietary Names for Pharmaceutical Substances  
Geneva, 19-22 October 2021 (virtual meeting)**

***Executive Summary***

***Programme on International Nonproprietary Names (INN)***

***INN Programme and Classification of Medical Products Unit  
Health Products Policy and Standards Department (HPS)  
Access to Medicines and Health Products Division (MHP)  
World Health Organization, Geneva***

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# **73<sup>rd</sup> Consultation on International Nonproprietary Names for Pharmaceutical Substances**

**Geneva, 19-22 October 2021 (virtual meeting)**

## **EXECUTIVE SUMMARY**

### **OPENING REMARKS**

On behalf of WHO and the ADG, Dr Clive Ondari, Director, Health Products policy and Standards (HPS) welcomed all to the 73<sup>rd</sup> INN Consultation. He expressed his gratitude to all experts, advisors and members of special agencies for their specialist advice to the INN Programme, a task made harder by having to work virtually, and everyone's patience was appreciated. He recognised the close working arrangements that had been forged over the years and the different ideas that emanate from the different scientific backgrounds, which gives strength to the Expert Group, and the close working relationship everyone has with the INN Secretariat; it would be a great loss if these contributions declined. He hoped that soon everyone would be able to work again face-to-face.

During this Consultation, he highlighted that there were 301 requests to discuss, 278 of these being new requests with 171 for biological substances and 107 for chemicals. Amongst these are 17 COVID-19 related substances. In addition to this huge work load, there are various policy issues to discuss including new nomenclature for mAbs and avoiding INN and TM conflicts. Dr Ondari was also aware of the extra meetings that had taken place between Consultations, working group meetings, the INN Open Club, and many other exchanges. Dr Ondari also expressed his gratitude to the INN Unit Head and the entire INN team; it is a small team but delivers an enormous punch.

Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products, thanked Dr Ondari for his kind words and the support he provides to the INN Unit. She added her own welcome to the experts, special advisors and participants from various agencies. She expressed her gratitude to them and to the INN team as a whole, whose abilities make life so much easier for her.

### **ELECTION of CHAIR, VICE-CHAIRS and RAPPORTEUR**

Prof. Sarel Malan was proposed and seconded for the role of Chair, and was so adopted. The appointments of Prof. Menico Rizzi as vice-chair for biologicals, Mr Adrian Evans for vice-chair of chemicals, and Dr James Robertson as Rapporteur, were similarly supported and adopted.

### **OPENING REMARKS (cont'd)**

The Chair thanked everyone for their confidence in him and Dr Ondari for his continued support; without his leadership the Programme would not function. He stressed that the experts and advisors work on INN because it is the right thing to do but enjoy it also. He proffered his thanks to Dr Balocco and her excellent team which has done so much in preparation for these meetings, and to the experts and advisors for their extensive work and comments prior to the meeting. With 301 requests to consider, time keeping will be essential;

there may not always be agreement, but the decisions of the Group are important for patient safety.

Dr Clive Ondari added congratulations to the chairs and vice-chairs for their election and leadership for this 73<sup>rd</sup> Consultation, and the rapporteur for his work. He was aware of the discussion on biosimilars at the earlier Open Session for Stakeholders and highlighted that the Group does not have to wait for orders from higher up to continue this dialogue, and that a gentle gradual re-opening of dialogue would be welcome. A few independent systems for biosimilars are emerging globally and that is not good.

The Chair thanked Dr Ondari for his comments and agreed that a soft approach would be useful for discussing biosimilar nomenclature.

## **CONFLICT of INTEREST**

A potential conflict of interest was declared by an INN Expert due to the Expert having recently co-authored a scientific paper alongside employees of a company submitting a request for an INN. The Expert would abstain from discussion of this particular request.

## **72<sup>nd</sup> NOTES of CONSULTATION**

The Notes of the 72<sup>nd</sup> Consultation were adopted as a fair reflection of the meeting and the Chair thanked the Rapporteur for his work. The Secretariat highlighted that the Notes represent a full record on the meeting, remain an internal document and should not be distributed outside of the Consultation. An Executive Summary has been published on the INN website.

## **NOMENCLATURE of INN**

During the 73<sup>rd</sup> INN Consultation, a total of 301 INN requests was discussed, including:

- 278 new INN requests, including 170 for biological substances
- 23 outstanding requests

As a result of these discussions, 287 names were selected, which are planned to be published in Lists 126 (COVID-19-related requests only) and 127 of proposed INN (p.INN). Three requests were withdrawn by the applicants, 1 request was INN (INN modified), 4 requests did not fulfill INN criteria (No INN) and 6 requests were deferred for future discussion.

Two new stems/substems were selected, 5 suffixes were promoted to the pre-stem list and it was decided to review the descriptions of 5 stems/pre-stems.

## **NEW SCHEME for MONOCLONAL ANTIBODY NOMENCLATURE**

At the 72<sup>nd</sup> INN Consultation a new nomenclature scheme for monoclonal antibodies (mAbs) was proposed and in the intervening period an INN mAb working group met several times to refine the original proposal. The current proposal presented to the INN Expert Group was to divide mAbs into four groups, with suffixes as follows:

- Group 1 comprises mAbs that are mono-specific and unmodified. Previously it was proposed that they would retain the *-mab* stem; however, given that other types of mAbs would have novel suffixes, it was felt best to drop the *-mab* stem altogether to avoid any

confusion or misunderstanding. An alternative suffix *-tug* or *-cab* for mono-specific and unmodified mAbs was proposed.

- Group 2 comprises mono-specific, full length mAbs that have an engineered constant domain, and would be named with a *-bart* suffix, for ‘antibody artificial’.
- Group 3 comprises bi- or multi-specific mAbs, regardless of their format, type or shape, and the suffix *-mig*, for multispecific-immunoglobulin was proposed, as before.
- Group 4 comprises mAbs that are monospecific fragments of any kind, and that are derived from an immunoglobulin variable domain, and the suffix *-ment* for fragment was proposed.

For infixes, it was proposed that *-ki-* for interleukins is enlarged to include all cytokines and cytokine receptors, and that the new proposed infixes *-sto-* and *-pru-* would be used for immunostimulatory antibodies and immunosuppressive antibodies, respectively. On the other hand, the infix *-li-* for immunomodulatory should be abandoned.

For Group 1 mAbs, *-tug* was preferred by most of the working group over *-cab*. The suffix *-tug* would represent a clean break from *-mab*, and currently there is no INN ending ‘ug’ and only two INN having ‘tug’ internally; the only disadvantage is that it would not be recognised easily as a mAb. It is easier to relate *-cab* to *-mab*, but already 800 INN end with ‘ab’, while 42 INN have ‘cab’ internally. Also, as *-cab* sounds a bit more like *-mab* it may be viewed as the only mAb group. It had been a challenging and demanding effort by the mAb working group, but the final proposal to the INN Expert Group was to divide mAbs into four groups as defined above with suffixes *-tug*, *-bart*, *-mig* and *-ment*, respectively.

*In discussion*, the thinking behind *-tug* was queried. This new suffix was primarily a random choice of letters presenting minimal conflict with other names and trademarks, and with respect to a definition it was agreed that the ‘ug’ part of *-tug* should stand for unmodified immunoglobulin.

The working group was also queried as to how this new scheme would be disseminated to stakeholders. It was highlighted that when the definition of a humanised mAb was changed, industry felt that it had been poorly communicated, and it was suggested that the INN Secretariat should lead a proactive official communication regarding this new scheme. The Secretariat noted that this was in hand with two options, a short letter to a scientific journal and a more comprehensive review of mAb naming and names given so far. The Secretariat also highlighted that the proposals had been discussed with the mAb working group of the IFPMA (International Federation of Pharmaceutical & Manufacturers Associations) and that they were supportive of it.

It was further discussed whether mAbs within the current batch of requests should be named with the *-mab* stem or with the new proposed scheme. With 93 new mAb requests, given the current difficulties in adopting unique mAb names, it was felt better to name the current requests using the new scheme and not wait until the new scheme had been communicated to stakeholders, but that a communication to stakeholders needs to be rapid and clear.

The Chair requested acceptance of the new scheme by the INN Expert Group and this was given (via electronic communication). It was also agreed to apply the new scheme to the requests being considered at this Consultation with the exception of USAN requests for

COVID-19 associated mAbs for which a USAN name has been agreed, as it would not be appropriate to change the tentatively agreed name for these at this stage.

The Chair thanked the working group for their efforts.

## **INN and TRADE MARK CONFLICTS**

INN need distinctive, memorable names that should not be liable to confusion with names in common use and a subgroup of Experts had assessed how potential conflict between proposed INN and trade marks should be assessed. There are more than 3.8 million trade marks (TM) registered with the World Intellectual Property Organisation (WIPO) as Nice Class 5 (pharmaceuticals and others), whilst there are more than 12,000 INN. Thus, considerable effort is required to create distinct INN. Similarity between INN and TM can be assessed by comparison of the first 5 letters, use of the POCA (Phonetic and Orthographic Computer Analysis) score, similarities at beginning and end of names, differences in vowels that may cause confusion in handwriting, and similarities with well-known medicines (cognitive errors). Examples of similarities include Rabexib™, a class 5 TM issued in 2021 and which is similar to the INN *rabeximod*, with the first 6 letters being identical, and the class 5 TM Sakuvitril™ (2021) which is very similar to the INN *sacubitril*, which begin with only 2 identical letters but overall, they are highly similar. The 5-letter rule itself was felt to be too wide but at the same time can miss relevant conflicts such as Sakuvitril™ versus *sacubitril*.

Looking at further INN principles, names proposed by the applicant should receive preferential consideration. Assessing TM conflicts should include assessing look-alike or sound-alike names, whether the TM is in a granted marketing authorisation, the degree of similarity, the medical setting and the legal status; ultimately it should be assessed if the names can co-exist safely. A decision tree was constructed incorporating these aspects with an emphasis on a safety review involving the indication, the type of prescription, the medical setting and the patient population. This decision tree would be for internal use only, will be subjective to a degree, and would need to be applied on a case-by-case basis.

*In discussion*, a biological advisor offered the use of a system they had developed based upon an algorithm used for comparing protein amino acid sequences, and this was felt to be useful.

In a virtual show of hands, the use of the decision tree was highly supported by the Experts.

## **EMA NAMING of COVID-19 VACCINES AGAINST VARIANTS of CONCERN**

In June 2021, the EMA Labelling Office issued a consultation on the naming of medicinal products containing COVID-19 vaccine variants, taking onboard the WHO announcement of simple, easy-to-say labels for SARS-CoV-2 Variants of Interest and Concern (VOI's and VOC's) using letters of the Greek alphabet, spelled out in full. The INN Programme responded to the EMA consultation in August and received a reply from the EMA in September.

The proposed EMA labelling depends on the naming structure but in each case would incorporate the WHO Greek letter label. Thus, for example, for a structure based upon the INN + marketing authorisation holder (MAH) the name would be the INN + WHO label + MAH. Due to space limitations on the immediate packaging, the WHO label would be reduced to a single Latin letter corresponding to the Greek letter (e.g. A for alpha), and this

would appear also on other materials alongside the full Greek letter. For vaccines that target multiple strains, each strain would be indicated in the labelling.

In the INN Programme response to the EMA labelling consultation, the EMA was encouraged to use the INN for COVID-19 vaccine variants and the EMA gave re-assurance that incorporation of the INN would indeed be enforced when available, although introduction of an INN post-authorisation is challenging, but that the agency was working on that. The Programme also highlighted to EMA that a labelling system based on the Greek alphabet posed some challenges, for example it would be difficult to distinguish between 0 (zero) used for the original Wuhan strain and O for the Greek letter Omicron. The Programme further highlighted to EMA that the protein INN nomenclature scheme already uses Greek letters to differentiate between glycoproteins and this could be problematic with a glycoprotein-based vaccine. For both of these situations, the EMA agreed there was potential for confusion and plans to address labelling on a case-by-case basis; once the relevant single Latin letter for the WHO Greek letter label had been agreed for a particular vaccine containing a VOC, the information would be published as an annex to the procedural guidance.

Further concern was expressed to the EMA that for multi-variant vaccines, the string of Latin letters representing the different Greek letters could be confused with other nomenclature systems such as the 4-letter codes used in the US for biologics and biosimilars. However, the EMA did not anticipate any issues as these 4-letter codes used in the USA are not included in EU applications. Finally, the INN Programme highlighted that any change in structure would require a new INN and the EMA reassured the Programme of its commitment to ensure INN are implemented in the product information, including for vaccine variants, when available.

The EMA representative present at the Consultation thanked the INN Experts for their input to the guidance on naming of products containing COVID-19 vaccine variants and confirmed that these have been carefully considered and necessary amendments to the guidance will be introduced. The complexity of the situation and difficulty in developing a flawless naming scheme in the short time frame given was pointed out. It was stressed that the procedural guidance developed by the EMA addresses naming of medicinal products to provide necessary distinction where there is potential for several vaccine variants to be included under the umbrella of a single marketing authorisation. This does not interfere with naming of active substances and the representative confirmed that where an INN exists it will be used. In the absence of a recommended INN a common name for the active substance will be adopted and used. It was also stressed that timely availability of INN is of essence due to the complexity of introducing a name change post authorisation and it was further confirmed that implementation of the approved INN for already authorised COVID-19 vaccines was in progress.

## **NAMING DEUTERATED SUBSTANCES**

Deuteration (the replacement of hydrogen atoms with the heavier isotope deuterium) is always indicated in INN, generally by the use of the prefix *deu-*. As an exception, one previous INN for a deuterated substance [zilascorb ( $^2\text{H}$ )] indicated deuteration with the isotope symbol ( $^2\text{H}$ ) following the INN, while another one [fludalanine] used the vague infix ('*d*'). In the past, requests for INN for deuterated substances have been for substances with a pre-existing INN while more recently, there have been requests where no INN exists for the

non-deuterated substance. It is likely that there will be an increasing number of requests for deuterated substances.

Substances in which hydrogen has been substituted with deuterium are very similar in size and shape and show similar biological properties. The carbon-deuterium bond is stronger than carbon-hydrogen and so deuterated chemicals tend to have longer half-lives and it is preferable to link an INN for a deuterated substance with the INN of the non-deuterated counterpart where that exists. Ways in which deuterated substances should be named include the well-used *deu(t)-* prefix on a pre-existing or new INN, the incorporation of *-deu-* as an infix, or the use of a second word such as *xxdeuter*, where ‘xx’ could indicate the number of deuterium atoms. However, *deu-* used as a prefix may result in a very large number of INN all with the same prefix, and so lacks diversity. The use of the isotope symbol (e.g.  $^2\text{H}$ ) is usually used for radioactive substances whereas deuterium is a stable isotope.

At the last INN Open Club, it was suggested that the use of the prefix *deu(t)-* should continue for substances with a pre-existing INN, while for novel substances deuteration should preferably be indicated by the infix *-deu-* placed immediately before the stem. If neither of these options is appropriate, a second word approach or the addition of the isotope symbol ( $^2\text{H}$ ) could be an option.

*In discussion*, it was added that deuteration can indeed result in slower metabolism of the substance but only at selected sites. As such, deuteration is generally undertaken at specific loci that will result in a longer life of the molecule.

## **SoINN**

The SoINN Steering Committee (SC) met the day before the 73<sup>rd</sup> INN Consultation and the SC Chair reported back to the INN Experts. The SoINN website now exists in three languages: English, French and Spanish, while a version in Arabic is under development. Two members of the ATC Collaborating Centre in Oslo were present at the SC meeting as a course on the ATC DDD classification is scheduled for inclusion on the SoINN website. Some current courses are to be updated in particular those on monoclonal antibodies, advanced therapies and vaccines. In addition to various courses, the website has a section on ‘stem in a pill’ in which pharmacological classes are identified by their stem; currently nearly twenty of these are available. The SC anticipates a face-to-face meeting with pilot university sites in the Spring of 2022 and if this is not possible, at least one virtual meeting will be organized. The SC is being supported by two INN Experts fluent in Arabic while the University of Alcalá in Spain will be offered to join the SC.

A need to re-energise students was recognised as the change to online tutoring caused by the pandemic had resulted in students being less enthusiastic, and the SoINN could help with that.

## **COLLABORATORS’ UPDATES**

### **Agência Nacional de Vigilância Sanitária (ANVISA), Brazil**

ANVISA is the Brazil National Health Surveillance Agency with a responsibility for the Brazilian Pharmacopoeia. During the first half of 2021, ANVISA the rebuilding of all 14 committees of the Brazilian Pharmacopoeia, 13 of which are technical committees and 1 managerial, was completed, after a public call in which interested parties submitted their

resumes. Since July (2021), the committees have been recomposed and are now functioning with a five-year term until 2026, when the Brazilian Pharmacopoeia will complete 100 years.

The Brazilian pharmaceutical substances nomenclature committee (CTT DCB) has seven members, with the ANVISA representative at the INN Consultation being honoured to have been selected as one of them, and furthermore, was chosen as coordinator by his peers. The coordinator also has a seat on the Brazilian Pharmacopoeia managerial committee.

The CTT DCB has already had two meetings since August, where 78 new names of pharmaceutical substances were approved and have been made official by ANVISA.

### **British Approved Names**

The 2022 British Approved Names (BAN) book main edition was published in August (2021) and is now available. It contains a number of new INN for substances that are authorised for use in the UK. The BAN found it useful to participate in naming INN and to bring these names to the UK; it was good to see how many new names are coming through.

### **International Union of Pure and Applied Chemistry (IUPAC)**

IUPAC chemical and biochemical nomenclature can be found at <https://iupac.qmul.ac.uk> while enzyme nomenclature and other IUBMB nomenclature can be found at <https://iubmb.qmul.ac.uk>.

Also on the web, ‘Corrections, Modifications and Extensions’ to the Nomenclature of Organic Chemistry IUPAC Recommendations and Preferred Names (the Blue Book), which was published in 2013, is available at <https://iupac.qmul.ac.uk/bibliog/BBerrors.html> while an HTML and PDF copy of the Blue Book incorporating these corrections is available at <https://iupac.qmul.ac.uk/BlueBook>

The other change reported was on the nomenclature of flavonoids, reference Nomenclature of Flavonoids (Recommendations 2017) Pure Appl. Chem. 2018, 90(9), 1429-1486 and available online at <https://iupac.qmul.ac.uk/flavonoid>.

### **Pharmaceuticals and Medical Devices Agency (PMDA), Japan**

The JAN (Japanese Accepted Names) Expert Committee took place virtually three times in May, July and October (2021). Since April, 35 names have been published and an *ad hoc* meeting to discuss Covid-19 related substances will be held.

The JP (Japanese Pharmacopoeia) 18th Edition was implemented in this June, and its English version will be published this year. The Pharmacopoeial Discussion Group (PDG), which brings together the European Pharmacopoeia (EP), the United States Pharmacopoeia (USP) and the JP, with the WHO as an observer, held its annual meeting in October (virtually), hosted by the EP. The PDG put the finishing touches to its plan for extending PDG membership. The plan is intended to be announced by the end of this October, inviting other world pharmacopoeias to join forces in providing strong, science-based harmonised pharmacopoeial standards.

<https://www.pmda.go.jp/files/000243251.pdf>



## **Therapeutic Goods Administration (TGA), Australia**

The Therapeutic Goods Administration (TGA) has undertaken an assessment on the protection offered by certain COVID-19 vaccines that are administered in certain countries but not currently registered in Australia. It is based on individual assessment of published data and in certain cases regulatory information provided in confidence. This advice is subject to change as new information becomes available. The TGA has undertaken this work at the request of Government and this work will help inform decisions that will subsequently be made by Government to support incoming travel to Australia in the coming months. The TGA will continue to interact with international regulators, monitor the medical literature and update its advice when sufficient information becomes available that demonstrates particular vaccines provide sufficient levels of protection. TGA's assessment report can be found at [COVID-19 vaccines not registered in Australia but in current international use - TGA advice on "recognition"](#).

Australian consumers now require a valid prescription from any of Australia's 100,000 medical practitioners to import nicotine vaping products, purchased from overseas websites. Consumers are required to ask overseas retailers to include a copy of their prescription with the order. Australian Border Force (ABF) officials can stop goods at the border that they suspect are unlawful imports and refer them to the TGA for further investigation. Nicotine vaping products may be seized if there is no prescription provided by the importer, or enclosed in the package, and the goods may be destroyed and the importer fined. Consumers continue to require a valid prescription to purchase nicotine vaping products from Australia pharmacies. It remains, illegal for Australian retailers (such as tobacconists, 'vape' shops and convenience stores) to sell nicotine vaping products to consumers.

## **United States Adopted Names (USAN)**

The 2021 summer USAN Council meeting took place virtually on June 4, 2021. Names for 35 drug substances were reviewed and discussed. Ten new stems and infixes were approved and added to USAN's stem list. The stems *-gli-* and *-netide* had their definitions revised to harmonize with the INN definitions. Thirty-four new INN applications and 2 revised INN applications for proposed USAN were prepared and forwarded to the INN Programme to be discussed at the 73rd INN Consultation.

Through October 2021, USAN staff will have processed, researched, and made recommendations for 223 USAN applications and forwarded this information to the USAN Council for their review and selection. Also through October, 236 USAN will have been adopted for 2021. Revenue was realized for an additional 8 negotiations. Currently, there are approximately 191 active USAN negotiations.

The 2021 Winter meeting of the USAN Council is scheduled for December 3, 2021 and will be a virtual meeting. The agenda items and the negotiation summaries for this meeting are currently being prepared.

## **United States Food and Drug Administration (FDA)**

There was no new specific FDA news on nomenclature beyond noting that vaccines get named in-house at CBER, but that CBER works with INN and USAN for naming advanced

therapies. FDA staff have been working from home since March 2020 and it is not known when there will be a mandatory return to the office; restrictions on travel also remain.

On November 1, the FDA had an internal meeting to start the process of identifying candidates to eventually take over the job of FDA liaison to the USAN Council / FDA observer at INN consultations; it will likely be 1-2 years before the appointee completely takes over this position.

### **United States Pharmacopoeia (USP)**

USP is actively engaging with academic research centres, pharmaceutical innovators, generic manufacturers, and regulators to drive Pharmaceutical Continuous Manufacturing (PCM) standardization efforts and develop collaboration opportunities.

In efforts to improve its customer experience, USP launched a new eCommerce site on June 13 to replace the iStore. This new USP Store gives users more self-service options and makes it easier to order products online, track order status, and manage business accounts directly.

Starting in January 2022, the new USP Dictionary of USAN and International Drug Names will be based fully on G-SRS. USP is working closely with NIH developers on the new platform.

### **WHO Collaborating Centre for Drug Statistic Methodology**

During the year, the WHO Collaborating Centre for Drug Statistic Methodology, based in the Norwegian Institute of Public Health, assigned 110 new ATC (Anatomical Therapeutic Chemical) codes, 30 new DDDs (Defined Daily Dose), and 46 ATC code alterations, the latter being due mainly to the creation of a new ATC 3rd level classification for antibody drugs and antibody drug conjugates (ATC group L01F). The proposal for this new classification had been the subject of a recent hearing and was adopted without amendment as a good way to handle these drugs. A revision of the classification of the immunosuppressants (ATC group L04) is now being discussed and further subdivision in new ATC 4th levels is a possibility.

### **WHO Collaborating Centre for International Drug Monitoring, the Uppsala Monitoring Centre, Sweden (UMC)**

The UMC highlighted that assigning INN to vaccines is better for the pharmacovigilance community. In discussions with the EMA, it is not clear how vaccine INN will affect them, nor indeed other regulatory agencies worldwide, and the UMC will need to look into how the EMA's own vaccine naming scheme will impact pharmacovigilance. The UMC has also discussed biosimilars with some regulatory authorities, the impact of glycan modification and the extent of difference between biosimilars. The UMC also makes use of the Global Substance Registration System (GSRS) for the implementation of the ISO suit of standards regarding identification of medicinal products (IDMP).

### **World Customs Organisation (WCO)**

The WCO representative highlighted the continued cooperation between WCO and the INN Programme. Since the previous INN Consultation, the HS (Harmonised System) Committee approved the classifications proposed by the Scientific Sub-Committee involving 322 substances from INN proposed Lists 122, 123 and 124 (COVID-19 Special Edition). The

Scientific Sub-Committee will meet in January 2022 to discuss the classification of the 380 substances from the INN Lists 124, 125 and 125 Special Edition. The WHO will be invited to participate in the discussions providing the technical information and guidance for the Scientific Sub-Committee to be able to assign specific HS codes to these substances.

### **World Intellectual Property Organization**

The new guidance in assessing trademark and INN conflicts and the associated decision tree are very interesting. The impact of this will be seen once INN lists are published and trademark owners can know about the names adopted under the new guidance.

### **CLOSE of MEETING**

As a final point, the Secretariat announced that the annotated list of proposed new INN would no longer be created and distributed to Experts as all such information is now available online through the IDMIS system.

In closing the meeting, the Chair highlighted that 301 requests had been discussed and that doing so on a virtual basis had been a challenge, but that he was grateful to everyone for taking part and contributing and was especially grateful for the efficient and hard work by the INN team in bringing it all together.

The 74<sup>th</sup> INN Consultation will take place on April 5-8, 2022.

## **OPEN SESSION for INN STAKEHOLDERS**

### **73<sup>rd</sup> Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances**

**(a virtual meeting)**

**Geneva, 19 October 2021**

Guests, INN experts and advisors, and participants from associated agencies were welcomed to the Open Session for INN Stakeholders being held as part of the 73<sup>rd</sup> INN Consultation by Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products on behalf of the ADG and Dr Clive Ondari, Director, Health Products policy and Standards. Only one stakeholder was present at this meeting, the ASBM, whose persistence, dedication and excellent presentations at these sessions were to be admired. Within the limits of what the INN Programme can achieve, the Programme is very conscious of the need for clear nomenclature for all medicines but especially for biologicals.

#### **Alliance for Safe Biologic Medicines (ASBM)**

The ASBM highlighted a poster it had presented at the DIA 2021 Global Annual Meeting in June, entitled ‘A review of problems with pharmacovigilance programs and biologics’. The poster presented a review of published literature on the identifiability of biologics with a specific focus on adverse event (AE) reporting. This is an important issue to physicians and it is essential to learn from their extensive use of biologics and any difference in use between biologics and biosimilars. Although physicians tend to rely on brand names to report an event, often only the non-proprietary name was included, with no brand name, and so it can be difficult to know which precise medicine had been given. For example, in reporting AE’s for *infliximab*, in 2018, 18% of ADR reports in Ireland lacked the brand name, 35% of reports from EudraVigilance similarly had no brand name and in a 2020 Canadian review 37% of reports had no brand name. Some reporting is better than others, but the use of the brand name was clearly not universal. A WHO report, highlighted on a previous occasion, notes that inconsistent nomenclature remains a challenge. For example, around the world, 13 *infliximab* products have different brand names that are inconsistently recorded and this leads to misattribution of AE’s, inaccurate patient records and overall confusion. With the proliferation of biosimilars, the ASBM noted that this is a challenge that the WHO is uniquely positioned to address.

The ASBM poster also referred to the ‘Swiss Cheese’ model of accident causation used for example by air traffic controllers and nuclear power plants, which highlights the need for additional layers of defence. For brand names, the holes in that line of defence are that they are not always reported. Thus a need for additional lines of defence such as the NDC (National Drug Code) in the USA and the DIN (Drug Identification Number) in Canada; the additional layer of safety that would be provided by the INN’s proposed Biological Qualifier (BQ) is to be applauded.

Objections to the use of distinct non-proprietary names for biosimilars quote that they may imply inferiority, that they may undermine confidence in their use and may hinder uptake. However, in the USA where biologics and biosimilars are distinguished with 4-letter suffix, this is not the case. In a new ASBM survey of 403 physicians who prescribe biologics in

practice, a good majority did not think the FDA suffix implies inferiority while >90% expressed confidence in the safety and efficacy of biosimilars. Notably, US physicians were more comfortable prescribing biosimilars to naïve patients than their EU counterparts. It is important to note also that in the USA all biosimilars and reference products will eventually have suffixes in the product name.

As to whether the FDA suffixes had held back adoption of biosimilars, it was shown that *filgrastim* biosimilars had achieved an 80% share of the market, and that various mAb biosimilars have a good share of the US market and which is expected to be >50% within 2 years, with price and not nomenclature appearing to be the predominant factor in increasing biosimilar uptake.

Following the attention given to COVID-19, there is renewed interest in pharmacovigilance and the role of biologics nomenclature, and the ASBM has recently discussed nomenclature at a Seminar on Biosimilar Medicines sponsored by the Maltese Medicines Authority in August, at a World Drug Safety Congress Americas in October, in a panel on improving pharmacovigilance programs around the world, and will be discussing these issues at the World Biosimilar Congress Europe 2021 in November.

In summary, the ASBM concluded that even in advanced countries there is inadequate identification using the brand name only and using distinguishable non-proprietary naming will strengthen pharmacovigilance programmes. A concern that distinguishable naming via use of a suffix would imply inferiority and hurt uptake, does not appear to be borne out and the ASBM will continue to work with regulators on this issue.

*In discussion*, the Uppsala Monitoring Centre representative commented that the pharmacovigilance reports it receives are not only sorted by tradename but also by a qualifier and aggregated, for example, on *infliximab*. Japan has its own biosimilars naming scheme, the UK and Norway both switch easily between reference product and biosimilar whereas in Sweden it is more regulated and physicians cannot easily choose. This makes it difficult to appreciate the benefit of treating biosimilars as substances on their own or as generics which is why it would be interesting to know the details to see if biosimilars are working just as the reference substance; the field is very unclear, has been discussed for a long time and it would be wise to get somewhere, to assess if small differences between biosimilars are significant.

The Chair noted that there was a perception in some circles that the INN Programme's BQ proposal was closed, whereas essentially it is on hold, and requested the ASBM to continue the debate not only with the INN group but also to write to the Executive Board of the WHO. The ASBM representative appreciated the interest of the INN group in its work and would take onboard reaching higher up within WHO.

The Chair thanked the ASBM and participants for the discussion and closed the meeting.