

**76th Consultation on International Nonproprietary Names for Pharmaceutical
Substances**

Geneva, 28-31 March 2023 (hybrid face-to-face/virtual meeting)

FINAL

Programme on International Nonproprietary Names (INN)

Access to Medicines and Health Products Division (MHP)
Health Product Policy and Standards Department (HPS)
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EXECUTIVE SUMMARY

WELCOME

The 76th INN Consultation was opened by Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products. Dr Balocco gave a warm welcome to all, both those present face-to-face and those online.

ELECTION of CHAIR, VICE-CHAIRS and RAPPORTEUR

Mr Adrian Evans was proposed, seconded and adopted as Chair. Mr Evans continued with elections of office bearers with Prof. Menico Rizzi being elected as vice-chair for biologicals, Prof. Vicente Rodilla as vice-chair for chemicals and Dr James Robertson as rapporteur.

With several new members a tour de table was held along with personal introductions by new members

OPENING REMARKS

Dr Clive Ondari, Director, Health Products Policy and Standards (HPS) and Director of the INN Programme, expressed his gratitude for the additional work the elected office bearers had accepted. He also expressed his appreciation to experts and advisors for their dedication and work already performed before the meeting. He emphasised the WHO code of conduct whereby experts work independently from their institutions/agencies, that work is performed to the best of the experts' expertise and that a high level of integrity is maintained. He highlighted that of 271 INN requests to be addressed, 238 were new requests of which 149 were biologicals and 89 were chemicals. This shift from chemical to biological requests has been continuing for several years. There is a new procedure in place for COVID-19 related applications for which there are 15 requests. There would be a proposal to make cell therapy requests more user-friendly and this is welcomed from stakeholders. Work continues on disseminating INN involving the WHO data hub and the School of INN (SoINN); the SoINN is expanding and helping to promote INN to both young trainee and experienced pharmacologists, and is enhancing the safety of prescribing. Dr Ondari also thanked his colleagues within the INN unit, for Dr Balocco for her leadership, and the entire team which does an incredible amount of work.

The Chair thanked the Director for his remarks and expressed his gratitude for the increase in resources that were available to the INN Programme as with continued global pharmacological research, requests for INN will only increase.

75th NOTES of CONSULTATION

The Notes of the 75th Consultation were adopted without objection and the Chair thanked the Rapporteur for his very comprehensive and clear work.

NOMENCLATURE of INN

During the 76th INN Consultation, a total of 271 INN requests was discussed, including:

- 238 new INN requests, including 149 for biological substances
- 33 outstanding requests

As a result of these discussions, 264 names were selected, which are planned to be published in Lists 129 (COVID-19-related requests only) and 130 of proposed INN (p.INN). One request did not fulfil INN criteria (No INN), 2 had been withdrawn by the applicants and 4 requests were deferred for future discussion.

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

Cell Therapy Nomenclature.

Since the previous Consultation, a small group of Experts had met to assess how names for cell and gene therapy substances could be simplified. With some cell therapy substance such as CART cells already marketed and other cell types such as iPSC's in an early growth phase, what was clear is that many hundreds of cell substances covering a wide range of complexity including autologous cells, allogeneic cells and gene edited cells, are under development. For these, the INN programme needed to be prepared with useful and usable names.

To date, names have been assigned with infixes that try to reflect key properties of the cells. To assist with this, the application form for cell therapy substances had been revised to clarify the information to be provided. However, following on from the greater complexity in designing cells for cell therapy there has been an increase in complexity of names. Currently, a key aspect in creating a name for cells is how much information should be built into the name versus what should remain in the Definition.

Participants of the meeting were reminded about the current naming schemes for cell and gene therapy substances. Cell therapy substances are given a one-word name ending in *-cel*, with an infix to identify the primary cell type, along with a random prefix. Gene therapy substances are given a two-word name, with the first word referring to the nature of the transgene involved and the second word the nature of the vector delivering the gene into the target tissue. Cell-based gene therapy substances are also assigned a two-word name, with the first word again defining the nature of the transgene and the second word the nature of the primary cell involved. Various infixes are used to specify the gene of interest, the nature of the vector or the nature of the cell type implanted. The prefix for the second word in cell-based gene therapy substance is typically *auto-* for autologous cells or *allo-* for allogeneic cells. Thus, INN for cell therapy substances tend to have two words that are long and complex. In contrast the brand names for many approved cell substances are quite short and much more user friendly.

Potential means of reducing the complexity of these INN were presented. These could involve keeping random prefixes as short as possible whilst maintaining the uniqueness of a name, keeping infixes to one syllable and reducing the length of some current overly long infixes to one syllable. The prefixes *auto-* and *allo-* for autologous and allogeneic cell-based gene therapies respectively could be reduced to *au-* and *allo-*. A further more radical approach for gene therapy and allogeneic cell-based gene therapy substances could be to remove the random prefix from the second word. This however could have consequences for medication errors for example where the same gene but a different vector is used for a specific therapy.

It was noted also that the INN Programme had worked closely in the past with USAN and CBER on naming cell therapy substances and this harmonisation needed to continue.

In discussion, the Chair acknowledged that the INN Programme cannot work on this alone and required US agencies and others to be onboard. It was also suggested that some gene infixes could designate a family of genes rather than each gene having its own unique infix. Ultimately, full details of a cell substance will appear in the Definition as it is not possible to embed everything in the name.

The ideas presented so far remain a proposal and Dr Balocco intimated that the INN Programme would like to present this work to the June meeting of the USAN Council and gather comments from CBER and USAN. There may also be value in submitting a letter to Lancet to highlight the importance of cell substance names and the limitations of what information can be imbedded in the name. The US FDA representative at the meeting suggested an informal call between the INN Programme, CBER and USAN prior to the June Council meeting; this was felt to be a useful way forward.

In ending this report, the INN Expert leading this topic thanked colleagues for their contributions to the discussions.

SCHOOL of INN (SoINN)

The SoINN steering committee met the day before the 76th INN Consultation and the following report was provided by the chair of the committee.

A major achievement is that the SoINN platform is now available in Arabic. It had been difficult to achieve a version that was clear and understandable in different Arabic speaking countries as the Arabic language can show differences that can be relevant. This new Arabic translation was validated by a reading involving three different Arabic experts. The SoINN courses are now available in English, French, Spanish and Arabic. The next challenge is to have a Mandarin version, but some technical issues need to be resolved before considering this.

Statistics and consultation of the website¹ continued to show the same pattern observed over the past year, i.e., access and usage is mainly through MedNet rather than directly through the courses (about 5000 single accessions per month). The majority of accessions are to the English version versus other languages (500 vs. <10). There had been a long discussion on how to improve the frequency of visits to the website, but everyone had agreed that the availability of different languages was of key importance. More effort should continue to be given to targeting university students but also other important stakeholders, including health practitioners, nurses, pharmacists in their professional organizations at national level, and patient organisations. The SoINN chair highlighted that promotional work cannot and must not be carried out by the INN Secretariat. All members of the Steering Committee and indeed all members of the INN Expert Group must consider how best to make use of SoINN documents for different potential audiences and the chair was grateful to those who had already made suggestions in this direction.

A new course on chemicals had been prepared and distributed amongst the steering committee members; comments received are to be incorporated into a new version.

A meeting of Pilot Sites had been organized for 24-25 May at the University of Grenoble, France and the agenda was almost finalised. The meeting will be divided into a public part

¹ <https://extranet.who.int/soinn>

and a restricted part and will address topics ranging from roles of the pilot sites to new ideas to foster and improve the SoINN and the culture of INN. Various and numerous stakeholders are to be invited and suggestions of people or organizations to be included were to be welcomed. The main goal is to stimulate the pilot sites and to involve everybody as much as possible, including in dissemination of the SoINN.

Establishing the Hospital of Grenoble a "Friend of INN" is also an ongoing project. Within this framework, the SoINN would like to encourage students of a particular module to engage in marketing of the SoINN, for example, by producing posters for patients and the public to explain what is an INN and the advantages of using INNs; engaging the public would be especially important.

The SoINN committee has also been in contact with the FIP (International Pharmaceutical Federation) steering committee with the aim of participating in the next FIP meeting to present INN and the SoINN.

Finally, it was reported that the SoINN Committee is developing a project that aims to analyse the development of medicines based on 70 years of INN and correlating this with the list of essential medicines. This could identify how various pharmacological categories change with time and help identify needs for current and future scenarios.

The INN Chair thanked the SoINN Committee chair and expressed satisfaction that it was progressing well.

COLLABORATORS' UPDATES

Brazilian Pharmaceutical Substances Nomenclature Committee (CTT DCB)

Since the last INN meeting (Oct 2022), the Brazilian Committee for Nomenclature of Pharmaceutical Substances (CTT DCB), a committee of the Brazilian Pharmacopeia, had held four meetings, in Nov and Dec 2022 and in Feb and Mar 2023, during which 35 names were approved, all of them directly linked to a medicine registration process in ANVISA, the Brazilian Medicines Agency.

European Medicines Agency

The Agency wanted to explore possible solutions for assigning INN to COVID mRNA vaccines in an accelerated manner, beyond what had been published already by the INN Programme. The Agency had started discussions with companies on authorising vaccines against upcoming COVID strains, and one such applicant indicated that due to time constraints, it may wish to drop the use of the INN for a new strain; however, the EMA stressed that the INN should continue to be used to distinguish the various formulations coexisting on the market. Thus, it was important that the INN gets approved early, as the company will be freezing the first few batches and will have to label them beforehand, essentially at risk.

The Agency posed three scenarios for assigning INN to variant COVID vaccines:

1. The company waits until after the decision on the strain is made and then applies for an INN; this would require a further acceleration of the process to assign the INN within the current 6 weeks.

2. Companies could submit several INN applications in parallel for prospective strains that might be chosen whilst awaiting the final decision as to which strain should be included; this would ensure an INN is available once the strain to be used for the MA is selected.

3. Companies could submit a “generic” INN request covering multiple variant candidates.

The Chair, voicing his own opinion, felt that the timescale for the first scenario would be difficult. For scenario 2, many INN are already assigned in early clinical development even although the substance is not and does not get marketed; so option 2 is an option. For option 3, he highlighted that INN are accompanied by a definition and having an open definition would be quite a precedent.

The EMA also requested clarification on the timelines that may apply when changes are made to an mRNA COVID vaccine beyond strain adaptation, noting that the standard process likely would apply but if a reduced timeframe could be considered. It was replied that INN for COVID related substances are given priority treatment and special Lists for these are produced beyond the standard Proposed List of INN. But whilst the INN Programme can accelerate the process to a degree, the requisite 4 months period for objections to new INN would still apply, although the time to publication could be shortened to perhaps 6 months.

The EMA representative was asked if the Agency was applying a 30-day timetable for Type 2 variations for these vaccines with the reply that this would depend on when data were submitted and if further information required. For example, a variation submission of July 2022 was approved the following September and that 60 days overall is probably the maximum.

International Union of Pure and Applied Chemistry (IUPAC)

A new edition of the IUPAC ‘Orange Book’ had recently been published by the Royal Society of Chemistry; properly entitled ‘Compendium of Terminology in Analytical Chemistry’. This latest edition has taken into account the explosion of new analytical procedures and, at the same time, the diversity of techniques and the quality and performance characteristics of the procedures that are the focus of interest.

Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Japanese Accepted Names (JAN): from October 2022 to March 2023 the JAN Expert Committee took place virtually two times, and 21 names were published.

Japanese Pharmacopoeia (JP): supplement 1 to the JP 18th edition was implemented in December 2022. The Pharmacopoeial Discussion Group (PDG), which brings together the European Pharmacopoeia (Ph. Eur.), the Japanese Pharmacopoeia (JP) and the United States Pharmacopoeia (USP), with the WHO as an observer, held its interim videoconference on March 15th. The Indian Pharmacopoeia Commission (IPC) joined the meeting as a participant in the PDG pilot scheme for global expansion. The next annual meeting is to be hosted by the USP in October.

Therapeutic Goods Administration (TGA), Australia

On 17 February 2023, the Therapeutic Goods Administration (TGA) granted provisional approval to Moderna’s bivalent COVID-19 vaccine: *elasomeran* and *davesomeran* (SPIKEVAX Bivalent Original/Omicron BA.4-5) for use as a booster dose in individuals aged 12 years and older. This is the second bivalent vaccine targeting the Omicron BA.4-5

subvariants that had been provisionally approved by the TGA and followed provisional approval of Pfizer's COMIRNATY BIVALENT Omicron BA.4/BA.5 COVID-19 vaccine in January 2023.

To reduce the incidence of serious injury and death from intentional paracetamol overdose, an interim decision to reduce the maximum pack size for various paracetamol products had been published by the TGA in February 2023. Details of the decision can be found on the [TGA website](#).

Following a safety investigation by the TGA, 55 products containing *pholcodine* have been cancelled from the Australian Register of Therapeutic Goods and those on pharmacy shelves have been recalled. This is due to a link between *pholcodine*-containing medicines and an increased risk of anaphylactic reactions to certain medicines used as muscle relaxants during general anaesthesia.

Changes have been made to classification of *psilocybin* and MDMA (from Schedule 9 [prohibited substance] to Schedule 8 [controlled substance]) to enable prescribing by authorised psychiatrists. Details have been made available on the [TGA website](#).

After 10 years in the role and many outstanding contributions, the head of the TGA, Dr John Skerritt, will retire in April 2023.

United States Adopted Names (USAN)

The 2022 winter USAN Council (USANC) meeting took place virtually on December 2, 2022, with all 5 members of the USANC and 15 other participants. Names for 41 drug substances were reviewed and discussed. Six new stems and infixes were approved and added to USAN's stem list. Two stem definitions were revised. Meeting topics discussed included: a Negotiations Update, USAN website metrics, the October 2022 INN Consultation, ISMP and FDA's medical error reports and a COVID-19 drug substances update. The 2023 Summer meeting of the USANC is scheduled for June 2, 2023 and will be an in-person meeting.

Thirty-four new INN applications and 3 revised INN applications for proposed USAN were prepared and forwarded to the INN Programme to be discussed at the 76th INN Consultation.

From January to March 2023, USAN staff will have processed, researched, and made recommendations for approximately 70 USAN applications and forwarded this information to the USAN Council for their review and name selection. Through March 2023, 64 USAN will have been adopted. Revenue was realized for an additional 3 negotiations. Currently, there are approximately 148 active USAN negotiations.

United States Food and Drug Administration (FDA)

The Center for Drug Evaluation and Research (CDER) has a new director, Dr Patrizia Cavazzoni, who has terminated the remote working program and cleared staff for travel. The FDA representative's second 10-year term as FDA liaison with USAN expires in the spring for 2024, and with travel restrictions lifted will now be able to attend the October INN Consultation in person. He had not been physically present at INN Consultations since 2019 and looked forward to doing so. Two staff members have been identified for continuing the nomenclature work, whom he will have to train, and one will probably start attending INN

Consultations next year. The FDA requires 90 days to process travel requests and kindly requested invitations being sent out as soon as possible.

United States Pharmacopoeia (USP)

The Small Molecules Chemical Information team, in collaboration with the Information Technology and Reference Standards Evaluation teams, had developed USP's Global Substance Registration System (G-SRS) as the central repository of chemical information across all USP publications. USP has transitioned to the G-SRS platform for curation of chemical information such as name, molecular weight, structure, as well as impurities. The G-SRS will provide a single source of USP's chemical information and would be leveraged by USP production processes that need to include chemical information. G-SRS will also assist agencies in registering and documenting information about substances found in medicines.

G-SRS is fully functional and available at USP and includes most of the impurity information given in current monographs. It also includes Potential Analytical Impurities (PAI)² for new products which do not have a monograph and will help manufacturers in developing new products.

World Customs Organisation (WCO)

The WCO representative highlighted the continued cooperation between the WCO and the WHO. Since the previous INN Consultation, the WCO Harmonised System (HS) Scientific Subcommittee (SSC) had examined the classification of 213 products of INN Proposed List 126 and pL.126 – COVID-19 (special edition) (plus addendum) and agreed on the classification of all but four substances - *esmethadone*, *imlunestrant*, *sirpefenicol* and *efrilacedase alfa*. At its recent 71st session, the HS Committee agreed on classifying *esmethadone* in HS code 2922.39 as an oxygen function amino compound whereas the remaining three substances are going to be further examined at the next session of the SSC. The SSC had also examined the classification of 250 substances of INN Proposed List 127 and pL.127 – COVID-19 (special edition) (plus addendum) and agreed on all of them. Moreover, it examined the classification of *larsucosterol* and *nendratareotide uzatansine* from List 124 and classified the former in sub-heading 2937.29 as a steroidal hormone derivative, and the latter in subheading 2939.79 as a derivative of *maitansine*, an alkaloid of vegetable origin. Finally, the classification of all *-fusp* ending proteins that had previously been classified by the HSC until the 37th session of the SSC, was also reviewed, and there was unanimous agreement with the previous classification of these INN substances in subheading 3002.13 as immunological products.

It was further emphasised that the WCO remained ready to work together with the WHO to classify new INN substances to assist in speeding up trade in these significant products and the Organisation was looking forward to discussing the classification of new INN substances that the WHO will submit to the next session of its SSC. The WCO also expressed its appreciation of the excellent contribution of Dr Lasseur of the INN Programme, who had

² Pharmaceutical Analytical Impurities are released using a process developed by USP's subject matter experts. The release process is based on internal policies, standard operating procedures, and requirements as defined by USP's Quality Management System. USP is an ISO 9001:2015 certified facility. PAI products are different from official USP Reference Standards and are not required for compendial compliance.

provided excellent technical information and guidance to the SSC during the discussions of the classification of INN substances.

Uppsala Monitoring Centre (UMC)

It was reported that after almost a year without a director, Dr Peter Hjelmström, a Swedish physician and research immunologist with an interest in pharmacovigilance, had been appointed director of the UMC. It was also reported that the Centre was heavily involved in the global implementation of the Identification of Medicinal Products (IDMP) standards and collaborates with a number of regulatory authorities on this. The UMC involvement focuses in particular on the pharmaceutical product ID, one of the IDMP standards. The extent of involvement of regulators varies widely but in general there is extensive interest and participation of them.

The UMC also works on the Global Substance Registration System (G-SRS) software, setting up a database for chemical drug substances with the USP, EMA and FDA in order to have a unique identifier for all chemical substances. Several other agencies are also starting to use this G-SRS software system. The UMC also works alongside the INN Programme on this. It was further emphasised that without INN, discussions on establishing the identifier would be far worse and that the INN is far easier to use by health care providers than a number. Finally, the UMC acknowledged that assigning INN to COVID vaccines was beneficial for good pharmacovigilance studies.

Changes to European Pharmaceutical Legislation

The meeting was informed of a proposed revision of European pharmaceutical legislation that the European Commission plans to publish on April 26th (2023) and of a Council recommendation on antimicrobial resistance under the concept of One Health. Publication of this proposal had been postponed several times already. In addition, the Commission planned to publish, also on 26th April, another package focusing on patents, that includes two important proposals, a one on compulsory licenses and a second on the revision of legislation related to the complementary certificate of protection.

With regard to EU pharmaceutical legislation, a leaked proposal for the revision had been circulating since February of this year. Current legislation includes Directive 2001/83 that established a community code on medicinal products for human use, plus Regulation 726/2004 that established the procedures for authorization and control of medicines for human and veterinary use, and creation of the EMA. There are two additional pharmaceutical Regulations, one for orphan and one for paediatric pharmaceutical products, and the proposed leaked version brings together these three Regulations into one. This new Regulation would also include a new definition for vaccines and immunological products, a new definition for active ingredients, as well as reference to INN. From this latter point, the INN group should consider compiling comments from an INN perspective.

The Chair expressed his appreciation on hearing about these changes.

CLOSE of MEETING

The Chair thank all participants for their contributions over four busy days of discussion and also expressed his gratitude to the INN Secretariat whose workload is increasing all the time.

Dr Balocco thanked the Chair for his excellent chairing of the meeting.

Next Meeting

The 77th INN Consultation will be held in Geneva on 17-20 October 2023.

OPEN SESSION for INN STAKEHOLDERS

76th Consultation on International Nonproprietary Names (INN) for Pharmaceutical Substances

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

Geneva, 28th March 2023

Dr Raffaella Balocco, Unit Head, INN Programme and Classification of Medical Products gave a warm welcome to all INN Experts, Advisors, and especially to Stakeholders to this Open Session of the 76th INN Consultation on behalf of the Assistant Director-General, a.i., Dr Hanan Balkhy, and Dr Clive Ondari, Director, Health Products Policy and Standards. The intention was to have an open discussion between stakeholders and the INN Experts and Advisors; however, she highlighted that it is 'open' only to those present at the meeting and any discussion should remain confidential until the meeting report is released. It was mentioned that unwelcome reports to the press of issues raised at these sessions had occurred in the past. The meeting was chaired by Adrian Evans.

Mr Evans, from the MHRA, UK, acknowledged acceptance of being the Chair. He was hopeful of having a fruitful and stimulating conversation, especially for gaining more understanding for naming of substances being addressed in the consultation.

Janssen Research & Development, LLC

At the 75th INN Consultation, Janssen's substance JNJ-77242113, an interleukin-23 antagonist peptide, was assigned the name *simtrokinra*, in contrast to the suggestions submitted by the company all of which had the suffix *-kintide* and with none of them having the *-tro-* infix. The suffix *-kinra* had been assigned by the Experts as the definition of this is 'interleukin receptor antagonist' with a '*-tro-*' infix for interleukin-23. The company, however, did not feel that the *-kinra* stem appropriately described JNJ-77242113, and provided argument as to why the stem *-tide* was more appropriate.

JNJ-77242113 is a small synthetic peptide containing natural and unnatural amino acids, which binds selectively to the interleukin IL-23 receptor (IL-23R) blocking the interaction of IL-23 with its receptor. It is similar to other unnatural peptides acting as receptor antagonists that have been assigned the stem *-tide* such as *motixafrotide* (120)(82), a small peptide chemokine CXCR4 receptor antagonist and *eptifibatide* (78)(40), a cyclic peptide acting as an antagonist of the integrin family receptor, α I**IIb** β 3, and of the fibrinogen receptor. In contrast, substances with the stem *-kinra*, although acting as receptor antagonists, have been developed for therapeutic indications different than the ones targeted by JNJ-77242113, are derived from naturally occurring proteins and generally are recombinant proteins and not peptides. Examples are *anakinra*, *pitrakinra* and *isunakinra*. An exception is *erepdekinra* (pL128) which is a peptide, but which consists of only natural amino-acids that include shared key amino-acid sequences with *anakinra* and *isunakinra*.

A further objection to the assigned name *simtrokinra* was that the *sintro-* random prefix of the word was too close to Sim-Trol, a herbicide containing simazine which has been banned in most European countries due to concerns for human and animal health and therefore

believed that a new prefix was necessary to avoid such conflicts. The company requested that the Experts reconsider the name and requested that a name making use of a *-trokintide* infix/suffix stem combination, which references both the IL-23 receptor target and the peptide structure be considered and selected at the 76th Consultation and provided suggestions with alternative prefixes.

In discussion, the company was asked about the pharmacological action of its substance compared with other antagonists, regardless of structure. The company highlighted that some IL-23 antagonists display different mechanisms of action, for example some bind selectively to different cell types. JNJ-77242113 does not bind to the Fc portion but binds directly to the IL-23 receptor. The company had no information on second messengers. One further difference though compared with other antagonists is that the substance is administered orally and not sub-cutaneous like most others.

EpiEndo

EpiEndo presented its non-antibiotic macrolide platform that addresses chronic epithelial disease and requested that the INN Experts consider its novel naming proposals for this new class of non-antibiotic macrolactones that demonstrate epithelial barrier-enhancing properties. The company proposed two new suffixes, *-barolide* (for epithelial **barrier** enhancers, **macrolide** derivatives) and *-mactel* (for non-antibiotic **macrolide** therapeutics; **epithelial** enhancers) and suggested six new names using these suffixes.

Epithelial integrity is key to inflammation. A breakdown in epithelial barrier function results in acute granulocytic inflammation which can lead into a continuous cycle of increasing inflammation in many epithelial diseases, such as COPD and asthma. Based on the macrolide antibiotic *azithromycin*, which shows epithelial anti-inflammatory activity, the goal of the company was to develop substances that maintain the anti-inflammatory but not have the antibiotic effects. This was achieved initially by screening a range of macrolactones against common airway bacteria and compounds void of antibacterial activity taken forward. The lead candidate EP395 showed superior barrier protective properties over *azithromycin in vitro*, and positive anti-inflammatory effects including those caused by viral infection. Indeed, EP395 will restore epithelial integrity by strengthening cell junctions, reducing the need for granulocyte stimulation, and thus help break the cycle of chronic inflammation.

The company highlighted that some macrolactones have epithelial barrier enhancing abilities that are completely unrelated to their antimicrobial effects, and that with several inflammatory diseases being characterized by underlying damage in the epithelial barrier, it is possible to create macrolactones that have barrier repair capabilities but without causing bacterial resistance and disruption of the microbiome.

The company also highlighted the many features of *barriolides* that do not fit into any existing INN class such as *-mycin*, *-imod*, *-emcinal* and *-olimus*., thus the request for a new suffix such as *-barolide* or *-mactel*.

In discussion on the mechanism of action at the molecular level, it was highlighted that such data had been sought for erythromycin for two decades. *Barriolides* have immunomodulatory effects believed to be a result of their positive charge interacting with negative aspects of the cell membrane, resulting in multi-factorial actions within the cell. Current data suggests that specific action is closely related to tight junctions.

Alliance of Safe Biologic Medicines (ASBM)

ASBM highlighted that with more biologics entering the marketplace, especially in ophthalmology, the need for accurate identification continues. In a recent letter, recommendations by the IFPMA focused on safe substitution of biologics by pharmacists and the associated need for accurate traceability. However, policies regarding automatic substitution differ widely between countries, ranging from being permitted for ‘interchangeable’ biosimilars only, to being generally permitted.

The ASBM had often expressed concerns regarding the substitution of biologics and this continues with the increasing use of such medicines in ophthalmology, for example *bevacizumab*. Five *bevacizumab* products are available in the USA, all with different proprietary names and distinct identifying suffixes but which cannot be substituted without physician involvement. However, in Canada, seven *bevacizumab* products are available but with no unique identifiers and automatic substitution by third party payers is increasingly common. As noted in the past, ASBM surveys have long shown strong support among physicians for distinct biologic nomenclature, including in Canada, in Latin America and elsewhere.

In a recent survey of prescribing practice by Canadian ophthalmologists, 20% prescribe by INN only, increasing the risk of inadvertent or inappropriate substitution. This is consistent with what has been observed before in its surveys worldwide. Similar results have also been obtained in surveys of adverse event reporting in Canada, and, as the INN is shared by multiple products (i.e., an originator and an ever-increasing number of biosimilars), this makes accurate attribution challenging. Furthermore, only 2% of Canadian physicians make use of the Drug Identification Number (DIN). Similarly, over 20% of Canadian AE reports rarely or never include the batch number. Analysing this Canadian data with the Swiss Cheese Model, about 20% would result in an event in which the exact product could not be identified as the brand name, DIN and batch number are not adequately used. In a final comment on the Canadian ophthalmology survey, 88% would support distinct naming.

In summarising, the ASBM highlighted again the need for and benefits of distinct naming. Physicians and manufacturing groups continue to have these concerns especially on pharmacovigilance, the impact of biologics cost and access. Support for distinct naming and international harmonisation continues and country-specific approaches remain inadequate. Ten years ago, the WHO INN Group proposed the BQ scheme and many countries would adopt a WHO international standard. With a continued proliferation of biologics and price reductions, the value of strong pharmacovigilance grows and the need to have confidence in these and substitution practice increases. Once again, the ASBM called for the WHO to lead distinct naming and the ASBM remained ready to assist in any programme.

Close of meeting

The Chair thanked the stakeholders for their presentations; they provided much food for thought on understanding how the INN Group should approach naming new medicines, and with that, the session was brought to a close.