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56th Consultation on International Nonproprietary Names for Pharmaceutical Substances Geneva, 15-17 April 2013

Executive Summary

Programme on International Nonproprietary Names (INN)

Quality Assurance and Safety: Medicines (QSM)
Essential Medicines and Health Products (EMP)
World Health Organization, Geneva

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EXECUTIVE SUMMARY

WELCOME AND INTRODUCTION

The 56th INN Consultation was opened and participants welcomed by Dr Lembit Rägo, Coordinator of Quality Assurance and Safety: Medicines, on behalf of the Director-General. Despite considerable reform within WHO, the INN Programme remains a stable core function. The Programme sits in a new cluster – Health Systems and Innovation – alongside regulated product streams including vaccines and other biologicals, Quality Safety and Standards, and devices including diagnostics. Challenging opportunities lie ahead and for the INN it is not an easy task to develop a clear strategy for biological medicines, but the INN has much to offer society, from patients through to all health-care professionals. Dr Rägo expressed his gratitude for the hard work of the experts and emphasized the need to maintain expertise in the future by considering next generation INN experts.

The Chair, Prof. Derek Calam, was grateful for those welcoming and informative words. There are challenging items on the agenda including a special meeting to discuss biosimilars. The world of biological medicines is indeed becoming increasingly complicated, is a challenge to the Experts, and echoed the need to identify appropriate experts whose opinion can be called upon in designing clear short names for very complex materials.

The Manager of the INN Programme, Dr Raffaella Balocco-Mattavelli, similarly welcomed participants and offered her thanks for the incredible amount of work achieved by the Experts prior to the Consultation itself.

NOMENCLATURE of INNs

During the Consultation, a total of 91 INNs were discussed, including:

- 70 new INN requests, including 31 for biological substances
- 17 outstanding requests
- 4 previously selected proposed INN, against which a formal objection had been raised

As a result of these discussions, 79 new names were selected, which are planned to be published in List 110 of Proposed INNs, while 2 requests were deferred for future discussion. Four requests were rejected by the INN experts, as the substances did not conform to the criteria for INN selection. Four amendments are planned to be published in List 110. Three new stems have been selected and 3 suffixes have been promoted to the pre-stem list.

UPDATE on FDA TAGS

The assignment of tags to two established INN by the US FDA (*ziv-aflibercept* and *tbo-filgrastim*) has previously been discussed, with there being no decision yet by the FDA as to whether or how to incorporate these tags into USAN. The Expert Committee were informed of a third such event, the assignment of the tag *ado-* to the conjugated monoclonal antibody *trastuzumab emtansine* on the basis of safety to distinguish it from the unconjugated product *trastuzumab*. The FDA representative explained that an option for the FDA had been to reverse the order of this two word name, but with many conjugated antibodies in the pipeline it was felt better to use a tag instead; in the meantime the FDA will be dealing with these on a case-by-case basis. Both *trastuzumab* and *trastuzumab emtansine* are owned by the same company for the same indication; they are not biosimilars or related

biologicals and the tag was introduced for safety reasons despite the USAN/INN names having been around for several years.

This event is of concern for two reasons. First, it suggests that the INN use of two word names presents a safety issue. The word *emtansine* is very strong and clinicians know that it is toxic; adding a prefix tag would be unlikely to solve any safety issue. Second, specific modification of the rINN outside of the INN Expert Committee is cause for concern. Other jurisdictions have made additions to the INN, e.g. in the UK when recombinant biologics were first adopted the cell origin was indicated by a three letter code and it remains a legal situation in the UK; a system in Japan exists also for biosimilars. In these cases qualification has occurred by addition of information rather than modification of the rINN. There is also apprehension that the FDA will continue in the future to review and tag such names, although the situation might be different where the unconjugated mAb is not on the market, unlike *trastuzumab* which is.

It needs to be emphasised to stakeholders that the INN Committee has a role given to it by the WHO Executive Board to devise a nomenclature system and a mechanism is in place for putting forward draft names and resolving potential problems before a name becomes recommended, and with the expectation that once a name has been adopted it is not changed or modified, unless deemed highly justified.

A letter had been sent at a high level from WHO to the US Government concerning this, but it might be better on both sides to identify someone in FDA who would review names from a safety point of view early in the process, prior to them becoming recommended INN, and working closely with that person(s). The addition of these tags has no doubt been done with best intentions but without realizing the impact on INN. There are other ways of flagging concerns that should be explored. The Expert Committee itself could also write to the FDA concerning this and is likely to have more impact than a letter from the INN Secretariat; perhaps a letter from the Director-General to government health departments should also be explored.

DRAFT INN NOMENCLATURE SCHEME for CELL THERAPY

In the draft INN nomenclature scheme for cell therapy products, it is proposed that *–cel* would be the common stem with a preceding infix that would designate the cell type, this basic approach being in line with the USAN scheme. A variety of infixes for different cell types would be created e.g. *–ep(a)–* for hepatocytes, *–de(n)–* for dendrocytes, and *–fi(b)–* for fibroblasts. Stem cells would be indicated by the infix *–tem–*, combined with a preceding second infix indicating the origin of the stem cell, i.e. *–atem–* for adult stem cells, *–etem–* for embryonic stem cells, *–otem–* for foetal stem cells, and *–utem–* for umbilical cord stem cells. Infixes could also be designated for tumour cell types, e.g. *–col–* for colon tumours, *–mel–* for melanoma, and *–glio–* for glioma.

Alternatively rather than indicate the precise tumour origin of a cell, *–tu–* could be used to cover all tumour types. Each name would begin with a fantasy prefix.

For genetically modified cells, a two word name is proposed. The first word would indicate the nature of the gene involved in the genetic modification and would be created in exactly the same way as in gene therapy nomenclature; the second word would indicate the cell and would follow the above scheme for cell therapy products.

The USAN has already created a nomenclature scheme for cell therapies and since 2005 has adopted fifteen names for cell therapy products. Comparing USAN adopted names with potential INN for the same cell therapy, INN in general were shorter and the final hyphenated letter in a USAN name would be absent. For example, the USAN Sipuleucel-T would be *sileucel* in the INN scheme, Carlecortemcel-L (USAN) would be *carutemcel* (INN), and Azficel-T (USAN) would be *azficel* (INN). For genetically engineered cell therapy products, the USAN is a single word name whilst the INN would have two words, for example, Lexgenleucel-T (USAN) would be *lerenvirogene buleucel* (INN).

Various aspects of this scheme were discussed. First, with respect to autologous, allogeneic and xenogeneic cell therapies, the inclusion of autologous cells in a naming scheme was questioned. It was felt that naming autologous cells was more akin to naming a process than a product, that autologous cells were more like extemporaneous compounding where a particular medicine is made for a particular patient, and as such were not amenable to naming despite some autologous cells being processed in a central facility far removed from the patient with consequent problems of labelling and export/import. These issues however were felt to be concerned more with traceability. Whilst no formal decision was taken, opinion was more in favour of not naming autologous cells.

There was reasonable agreement that details of cell manipulation should be in the Definition rather than in the name. However, for genetically engineered cells, the proposal includes aspects of the manipulation in the (first word of the) name. The need for such a two word name was questioned as the existence of a genetic manipulation step could be incorporated in the second word (thus removing the first word); but it was also questioned that if genetic modification was indicated in this way, should not other types of manipulation also be included within the name. Further, whilst it was agreed that there was little need to include the nature of the genetic modifying vector in the name for a genetically modified cell, only the modifying gene, the question of whether applicants should be required to apply for a separate INN for the modifying vector (which would be akin to a gene therapy product) was raised, especially as a single vector may be used in the modification of a variety of cell therapy products.

A final point for discussion was the issue of tumour cells and the need to learn from the mAb scheme in not having too many syllables in the name. It was opined that it was superfluous to include an infix for both the cell tumour type and the infix *–tu–*, with some preference for using the former and dropping *–tu–*.It was also suggested that an appropriate infix could indicate where a cell is being used as an anti-tumour vaccine owing to its antigen presenting cell function.

The *–CEPT* STEM - OVERVIEW of MEMBERS

The stem *–cept* is used for receptor molecules, both native and modified, and is preceded by an infix (substem) for different receptor types. Nineteen *–cept* INN have been assigned and fall into three groups – free receptor proteins (3 INN), conjugated receptors (2 INN) and fusion proteins (14 INN). For the two conjugates the nature of the conjugate is encompassed within the INN (one is pegylated to enhance half-life, and one is linked to a toxin). The largest group are the fusion proteins in which the receptor molecule is fused with an Fc fragment of IgG. Whilst the Fc moiety can confer effector functions of IgG such as phagocytosis of immune complexes, complement activation, or transportation through blood vessel walls, for all but one of the fusion proteins, the main reason for the fusion appears to be to make use of the PK enhancing features of the Fc fragment. However, whatever function the Fc portion confers upon the fusion protein, the presence of the Fc fragment is not specifically indicated in the INN (such as by the use of the prefix *–ef–*) and with fourteen already named, it is probably too late to do so.

An INN QUALIFIER for BIOSIMILARS

On the day following this 56th Consultation, a closed meeting was held on *Discussion on INN Proposal for Similar Biological Products (SBPs)*, attended by biological experts of the INN Expert Committee and representatives from worldwide regulatory agencies. As a prelude to that Dr Grant from TGA, Australia gave a presentation on a proposal for an INN naming scheme for SBPs. This was Dr Grant's personal proposal and is neither a TGA nor an INN Expert Committee recommendation.

INN for SBPs follow general naming principles and there are no specific means of identifying them as SBPs within their INN. The current naming situation is such that non-glycosylated SBPs have the same INN whilst glycosylated SPBs are likely to have a different name from their reference product

due to potential differences in their glycoforms, this being achieved by the use of a Greek letter, although in neither case is the reference product identified within the INN. Comparability studies get performed between an SBP and its reference product, but studies between one SBP and another are not done; two separate SBPs may have been compared to the same reference but not between themselves. Thus, switching between SBPs is not desirable and there needs to be some way of distinguishing between one SBP and another and between the reference product. Whilst this is a regulatory authorities responsibility, it is a clear mandate of WHO INN Programme to ensure clear identification of pharmaceutical substances, both chemicals and biological. Dr Grant and other experts felt that the best way to do this is through nomenclature with involvement of the INN programme in developing a unique global qualifier. Also, what needs to be avoided is for individual regulatory bodies to assign their own non-unified qualifiers.

The proposal is that an SBP should have a two part name; the first part would be the INN of the reference product while the second part would be a qualifier whose object is to say that this is an SBP and identifies it as a particular SBP. In Japan drug nomenclature, a biosimilar is denoted by 'BS' plus a name for the manufacturer and such an approach could be adopted by the INN Programme. A numbering system is also a possibility but is not compatible with INN policy. The approach favoured by Dr Grant is the use of a word identifier, e.g. *sim-* plus a fantasy suffix. If any of these three possibilities get used, WHO would be responsible for the identifier and assigning a fantasy suffix. To achieve this, WHO could assign the qualifier according to an agreed policy or alternatively WHO could produce a policy document by which regulatory authorities produce the fantasy suffix or code; Dr Grant's preference is for the INN Programme to have responsibility in naming SBPs. In the event the INN Programme issues an SBP qualifier, this would not necessarily identify the product as an SBP, it would simply mean that a sponsor has applied for a particular name for approval as an INN. The INN is a voluntary instrument but it is highly useful and the above scheme would be a means by which national regulators could identify a substance as an SBP/biosimilar.

The possibility to extend the use of the qualifier to all bioogicals, including SBP approved not as biosimilar, has been mentioned.

Discussion on this topic was deferred until the special meeting on SBPs at which the need for a systematic way of identifying biosimilars from different sources would be discussed.

UPDATES from COLLABORATORS

British Approved Names (BAN)

Supplement No 2 of the BAN is going to press in August (2013) and will be available in September 2013. A consultation with stakeholders is planned regarding the availability of the BAN in electronic format only.

Food and Drug Administration (FDA), USA

In the USA biological products are regulated through CBER according to the Public Health Service Act whilst chemical drugs are approved through CDER by the Food, Drug, and Cosmetics Act. Biologics regulated by CBER do not need to have a legal established name, unlike products authorised by CDER which do, as prescribed by the Food, Drug, and Cosmetics Act. The non-proprietary or established name can be some other name beyond USAN.

Most biologics in the USA are still patent protected but how to name biosimilars is under consideration and a bio-nomenclature working group is drafting guidance on this. International harmonization issues will be addressed in the guidance, but whilst it is in draft form there is very little else that can be said about it except that it will not cover the legal ramifications of naming. The guidance will be for the public and industry, will be amenable to comment and not be binding. It is difficult to forecast when it will be made public as it has to be signed off by numerous offices.

International Union of Pure and Applied Chemistry (IUPAC)

The update of the Blue book (organic structures) is progressing well and should go to press before the end of 2013; it will be a very large volume and is filled with cross correlations.

Pharmaceuticals and Medical Devices Agency (PMDA), Japan

The Division of Pharmacopoeia and Standards for Drugs within the PMDA is the Secretariat for both the Japanese Accepted Names (JAN) and the Japanese Pharmacopeoia (JP), and has responsibility for the preparation of JAN and for drafts of the JP. With sixteen members, the JAN Expert Committee is chaired by Dr Okuda (who is also an INN Expert Committee member) and considers applications on a quarterly basis. The number of submissions to the JAN averages fifty per year, with 15-20% comprising biologicals.

When an INN exists for a JAN submission, the Committee will confirm the INN as the JAN; if no INN pre-exists, a new JAN will be created with a recommendation to the applicant to apply for an INN. If an INN is subsequently provided and is different from the JAN, the JAN will be changed.

Supplement 1 of the 16th Edition of the Japanese Pharmacopoeia was implemented on 1 October 2012, whilst an English version will be available on the web site very soon.

Taxation and Customs Union (TAXUD), European Commission

The European Customs Inventory of Chemical Substances (ECICS) is an information tool managed by the EU Directorate-General for Taxation and Customs Union (DG TAXUD). It is publicly available via the Internet, free of charge and contains a large number of chemical and pharmaceutical products, their CAS RNs and their customs codes. A translation tool is almost ready which will provide translation of chemical names into all official EU languages.

INNs benefit from duty-free treatment upon importation in the EU if they are subject of the Pharmaceutical Sectoral Arrangement of the WTO concluded during the Uruguay Round (1994). This international arrangement was updated four times since then and includes >95% of the INNs from pINN lists 1-99. For example, certain plastics with an INN were not included as its inclusion would have huge impact on the respective industry. Similarly, levoglucose (INN) which was assigned recently an INN described as diagnostic aid is not likely to enter the list of duty free goods. Now the fifth revision of the Arrangement is about to be started which will most likely include the majority of INNs from pINN lists 100-107

United States Approved Names (USAN)

The 2013 Winter USAN Council meeting took place in Miami Beach, Florida in January, where names for thirty-three drugs substances were proposed. Seven new stems and one revised stem definition were approved and posted on the USAN website. Two designations for radicals and anions were approved and posted. Twenty-seven INN applications for proposed USAN were prepared for this 56th INN Consultation. Planning for the summer 2013 Council meeting has begun and is scheduled for 11-12 July in Chicago. Dr Armen Melikian was appointed to the USAN Council as the APhA representative whilst within the USAN Program itself Mary Haynes joined as an administrative assistant. By 13 March, USAN staff had processed 33 new USAN applications which were forwarded to the Council, and in the first quarter of 2013, 28 new, 11 modified and 3 revised USAN were adopted and revenue was realized for an additional 5 negotiations.

United States Pharmacopoeia (USP)

The USP is not part of the US government and is a not-for-profit private corporation. It predates the FDA by 100 years and for 200 years has been setting standards, with the FDA accepting decisions made by the USP. There is often confusion between the drug substance (DS) and the drug product (DP). The DS is what a company finds promising and brings to the INN for a non-proprietary name. In the USA, it is written in law that the USP confirms names for the DP and all drug products in the US market must conform to the standards in the USP-NF to avoid possible charges of adulteration and misbranding. The USP Nomenclature, Safety, and Labelling (NSL) Expert Committee, in addition to the FDA and the USAN, is also involved in approving an established name for the DS.

Shortly before this INN meeting, there was a meeting of the NSL Expert Committee at which it had hoped to discuss biologics nomenclature; however the FDA was not prepared to discuss this topic at that time. The USP salt policy goes into effect on 1 May 2013. The policy stipulates that for drugs containing a salt of an acid or base, the name of the active moiety excludes the counter ion, e.g. the active moiety of a metal salt of an acid, is the free acid. There was further discussion on quaternary salts and a decision was made to include these in the policy, and the FDA is on board with this.

Finally, it was reported that the USP has a new logo.

WHO Collaborating Centre for Drug Statistics Methodology, Norway

The Centre has recently had its semi-annual meeting and the minutes are waiting to be approved.

World Intellectual Property Organisation (WIPO)

The WIPO representative provided the Committee with an Article summarizing a Decision taken by the Swiss Federal Administrative Court on 4 March 2013 on the scope of protection of trademarks containing INN stems. In this case, the Swiss Federal Tribunal noted that under normal circumstances the registration of a trademark consisting of an INN would have to be refused, whereas there was no general exclusion to register a trademark that combined an INN or an INN stem with an additional distinctive element. In addition, the Decision also contained a paragraph describing the protection of INN under German case law as limited. According to the WIPO representative, the fact that the Swiss Federal Administrative Court dealt with INN stems showed that domestic courts and trademark offices had an increasing interest in INN stems. She highlighted that it was therefore important to make information on INN stems available and recalled that during the twenty-seventh session of the WIPO Standing Committee on the Law of Trademarks, Industrial Designs and Geographical Indications, held in Geneva from 18-21 September 2012, the Delegation of Denmark had asked whether a list of INN stems could be included in the INN Global Data Hub, in order to facilitate search and examination of trademark applications consisting of or containing INN stems.

Dr Balocco noted that the INN Secretariat had often written to trademark authorities requesting them to refuse the registration of trademarks consisting of INN and that awareness for the protection of INN was growing. National practices, however, diverged considerably, and Dr Balocco thus welcomed the information on the Swiss Federal Tribunal Decision. Dr David Lewis (USFDA) explained that when considering new pharmaceutical names submitted for authorization, the USFDA no longer authorized names that included INN stems. Dr Antonio Romeo informed the Committee that, following the request made by the Delegation of Denmark to the SCT, the INN Secretariat had introduced a possibility to search for two and three-letter stems in the INN Global Data Hub.

UPDATE on IDMIS SYSTEM

Online administrative tools within the INN Programme continue to expand, with a recent addition being the facility to check the similarity between proposed INN and other similar stem names, either for an exact match to a stem or with 1, 2 or 3 letter differences; this needs to be trialled by the Experts. For searching trademarks against stems, IDMIS is also being linked to a WIPO search tool.

The INN Global Data Hub has been successfully integrated to the CESTO database (Common examiner's support tool) based at the OHIM centre in Alicante. During the meeting was shown how the INN Hub will allow comparison of INN with CESTO for conflicts with TMs and prevent the abuse of INN by companies creating inappropriate trademarks

CLOSE of MEETING

The Chair closed the 56th Consultation thanking the Secretariat and the Experts for their hard work; all expert contributions are very valuable and are much appreciated. The Chair in turn was thanked for his efforts and excellent chairmanship.

NEXT MEETING

The 57th INN Consultation will take place in Geneva on 22-24 October 2013.

OPEN SESSION for STAKEHOLDERS

56th Consultation on International Nonproprietary Names (INN) for

Pharmaceutical Substances

Geneva, 16 April 2013

Stakeholders were welcomed by Professor Derek Calam, Chair of the INN Expert Committee. Stakeholders' open sessions began a few years ago in conjunction with INN Consultations to give applicants the opportunity to explain their applications in detail. General INN issues of concern can also be addressed and the scope of these open sessions has been broadened to include discussion of policy issues. Stakeholders were reminded that the remit of the Expert Committee is to develop names with non-proprietary rights but to bear in mind that the Committee is only able to make recommendations on applications and not to enforce their use.

The Programme Manager Dr Raffaella Balocco Mattavelli, welcomed the stakeholders on behalf of the Director and Coordinator of the Programme, Dr de Joncheere and Dr Rägo respectively. Unfortunately with six presentations, time is short, but this remains an important opportunity for open discussion between stakeholders and INN experts. As is the norm for WHO groups, names of experts remain confidential.

Allergan

Allergan argued for an INN for the commercial product BOTOX-R which has been on the market for 24 years. Botulinum toxin is a powerful neurotoxin derived from clostridium botulinum and used therapeutically in blocking overactive nerve impulses. In addition to BOTOX there are a variety of other Botulinum toxins licensed worldwide, none of which have an INN. Botulinum toxin type A products have a common core neurotoxin plus associated proteins, levels of which vary between the different products. These different preparations have unique properties and the EMA's Biosimilars Working Party has stated that serotype A botulinum toxins do not qualify as biosimilars due to obvious differences in physicochemical characteristics, dose and regimen. They are non-interchangeable and non-equivalent within the same indication.

Several have been assigned USAN that are used not only in the USA but informally in many other countries by a variety of agencies and widely in international publications. Allergan is concerned that the lack of INN for the different products could lead to medication errors, especially in dosing, and is confusing for health-care workers as they are often generically referred to as Botulinum toxin type A, or simply as 'Botox'. Thus whilst many prescribers appreciate these differences, with many products on the market, new brand names appearing, new indications and inconsistent use of USAN, there is a need to standardize and have INN assigned. Whilst this submission is specific for Allergan's BOTOX-R, others hopefully would follow.

It was noted that a previous decision not to assign an INN to BOTOX-R was because it was not clearly defined and clarification was sought by the Committee on the extent that 'botox' preparations are mixtures of two or more components.

European Generic Medicines Association (EGA)

The European Generic Medicines Association (EGA) addressed the Committee on the topic of new INN/INN identifiers for biosimilars. Its experience is that the current INN scheme works well within the EU and that the creation of new names/identifiers will cause confusion and constitutes a safety issue. Originator product manufacturers often change their manufacturing process, for example Remicade has gone through >35 manufacturing changes that resulted in post-translational changes but regulators have remained satisfied with clinical data showing comparability. In the same vein, when a biosimilar is shown to be physically and clinically comparable, the same INN (as the reference product) should apply. Conversely, where there are differences and products are not comparable then a unique INN is required.

The EGA also stressed that currently there are redundant means of identification whereby the brand name (used primarily by physicians) or the INN plus the manufacturer's name, both provide unique identification, and that the addition of a further suffix will not improve pharmacovigilance and may cause confusion. The INN was never intended to be used solely for pharmacovigilance; it is used for identifying the drug substance and not the drug product. Furthermore the use of a unique 'BS' suffix to the INN in Japan for biosimilars has been an impediment to patient access, whilst in Australia the use of the same INN for non-glycosylated biosimilars compared to the use of different INN for glycosylated biosimilars has resulted in differences in market penetration. In conclusion, the EGA felt that the current situation should be maintained, that regulatory authorities have experience that it is working, and if a product is a biosimilar then the same INN should be used but if biosimilarity is not shown then there must be a unique INN.

There was discussion about the naming and use of biosimilars in different regulatory settings, and their effect on market penetration; however, the INN remains a voluntary system which cannot be guided by market penetration, and different decisions on INN that have been taken by different regulators have all been in the absence of any consultation with WHO. The INN Programme remains committed to building harmonization and to listen and to apply a global scheme, to which the EGA was in agreement.

Ferring Pharmaceuticals

Ferring Pharmaceuticals had previously applied for and received an INN for its human recombinant follicle stimulating hormone (FSH) – *follitropin delta*. Follitropin delta is manufactured in a recombinant human cell line and has been shown to be structurally and clinically distinct from other follitropins on the market, all of which are synthesised in CHO cells. It has distinct glycosylation, isoelectric focusing pattern and, significantly, a unique PD/PF profile, resulting in a higher clinical potency and a dosing regimen based upon micrograms rather than the more conventional bioassay derived units. Indeed, both the EMA and FDA have acknowledged the exclusive and innovative nature of the Ferring product and have noted that it is clearly not biosimilar to other follitropins on the market. The company is concerned that the Greek letter suffix alone is not strong enough to prevent accidental or intentional substitution without appreciating the differing clinical strength of their product from other follitropins. Consequently, Ferring is arguing that a more distinct INN is required, one with a fantasy prefix in addition to the Greek letter suffix assigned to their FSH, with *antrofillitropin delta* being their preferred name.

In discussion it was suggested that a similar clinical disparity could be obtained for a CHO derived product using a stronger ion exchange column; however, Ferring did not have any evidence that differences in sialylation are responsible for the differing clinical effects. It was also raised that there is a precedent for other biopharmaceuticals deriving from CHO versus human cell lines being distinguished solely by Greek letter suffixes and it was reiterated that according to INN rules, for a protein with the same amino acid sequence, the same first word is applied. A decision on their reapplication will be taken during the adjoining 56th INN Consultation.

Novartis Pharma AG

Novartis presented details of a new drug for the treatment of Cushing's syndrome. This is a disease caused by a pituitary tumour resulting in the overproduction of ACTH, which in turn acts upon the adrenals to over produce cortisol. This excess of cortisol causes various debilitating morbidities including hypertension, obesity, diabetes, depression, and also excess mortality. There are various treatment options ranging from surgery or radiation targeting the tumour itself, to drugs targeting various receptors to interrupt the biochemical pathways that result in cortisol overproduction.

Novartis has a new inhibitor of steroidogenesis – LC1699 – an inhibitor of 11β-hydroxylase, the enzyme catalysing the final step in the biosynthesis of cortisol. Details of the structure of LC1699 alongside that of other drugs of the same class were provided. LC1699 has undergone initial clinical investigation, is well tolerated and is effective in achieving urinary-free cortisol over time.

A request for an INN for LC1699 had been submitted to the 55th Consultation; however, a decision on a name was deferred pending more detailed information on the drug including its mode of action.

The purpose of this presentation was to provide such information. Based on its structure, WHO has proposed the suffix *-talene* following the IUPAC name for two fused five-membered rings and Novartis proposed several INN with this suffix for consideration by the INN Committee at the 56th Consultation.

International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

The IFPMA shares the goal of the INN in having a clear globally harmonized naming scheme for biopharmaceuticals and welcomes the WHO plan to consider an identifier for SBPs/biosimilars. It is very important that biopharmaceuticals are identified clearly for prescribing and the IFPMA feel that this is not happening through INN usage. The INN Committee has also made it clear that they are not regulatory authorities and that the current situation for SBPs is not sustainable. An extra identifier is a possible solution but implementation is a crucial aspect as different authorities have different processes for naming and prescribing biopharmaceuticals. The issue is not about biosimilarity or not, but the need for clear identification, accurate dispensing and the role of INN in this scenario. The IFPMA see the key principles for achieving this to be that all approved biotherapeutics whether innovator or not, need to be individually identifiable irrespective of their regulatory approval, and that different SBPs need to be distinguished from each other and from the reference product. The IFPMA also see a lack of global uniformity as weakening the INN system and that NRAs will have to implement INN naming requirements regardless of the solution. Finally IFPMA agreed that the current system is not sustainable and action is needed.

The INN remains the most consistent piece of information for adverse event reporting but biotherapeutics require more than this. Lot numbers are not always reported, brand names are not always on the container and not all indications will necessarily be approved for a given biosimilar. Distinguishable INNs, including a unique identifier could be a promising global solution. The IFPMA is not keen on WHO encouraging regulatory authorities to provide an identifier as this could lead to different identifiers in different jurisdictions, weakening further the INN and increasing global confusion.

IFPMA supports the publication of a proposal for implementation of a distinguishable INN including an unique product identifier. It recommends that WHO develop implementing guidelines for the use of distinguishable INN to reinforce WHO's expectations from NRAs' application of a new system, for clarification of procedures for assigning a WHO-issued identifier, and to emphasise that any unique identifier is within labelling requirements. It does not believe that an unique identifier will achieve its objectives unless it is used alongside the INN and the sooner a solution is reached the better countries are working on and implementing their own identifiers and naming schemes.

Winston & Strawn

The representative from Winston & Strawn, a lawyer in intellectual property, did not give a formal presentation but instead informed the INN Committee that the aim of attending was to get a feel of the format of the meeting. He expressed interest in the allocation of INN to biosimilars and has followed the reports of previous meetings. He was heartened by the role of INN and the support the Committee provides and would welcome an opportunity to return.

Dr Balocco informed him of the INN training course held annually, usually in January each year, and in which he may be interested. The Chair expressed his opinion that perhaps there could be better publicity for the course and that maybe it could be held more often than annually.

Close of meeting

The Chair closed the meeting thanking all stakeholders present for their presentations, which provide useful background information which will be considered by the Committee in formulating future policy guidelines.