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International Nonproprietary Names (INN) for biological and biotechnological substances

(a review)

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International Nonproprietary Names (INN) for biological and biotechnological substances

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Programme on International Nonproprietary Names (INN)
Quality Assurance and Safety: Medicines
Essential Medicines and Pharmaceutical Policies (EMP)

International Nonproprietary Names (INN) for biological and biotechnological substances

(a review)

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0. INTRODUCTION

More than 50 years ago, WHO established the International Nonproprietary Name (INN) Expert Group / WHO Expert Committee on Specifications for Pharmaceutical Preparations, to assign nonproprietary names to medicinal substances, so that each substance would be recognized globally by a unique name. These INNs do not give proprietary rights, unlike a trade mark, and can be used freely as they are public property.

INNs have been assigned to biological products since the early days of the INN Programme. As well as many names for individual substances, animal insulin preparations were given an INN in Recommended list 3 in 1959. In the period up to 1980, names were assigned to antibiotics, synthetic peptides, hormones and other proteins. In names of compounds related by structure and / or function, specific letter groups, called stems, are included to aid recognition by health professionals. The -*actid*e for synthetic polypeptides with a corticotrophin-like action is an example.

In 1982, the name *insulin human* was proposed for the recombinant protein identical to natural human insulin, and since then names have been assigned to a growing number of recombinant products. Within the INN Programme, names have not been assigned to natural human blood products or vaccines. For those groups of biological products, the WHO Expert Committee on Biological Standardization (ECBS) has been adopting the scientific names of the biological products within the definitions of respective requirements.

Since the time when *insulin human* became the first recommended INN (rINN) for a recombinant product, the range of biological / biotechnological products has increased in size and complexity. For example, new stems have been introduced for tissue plasminogen activators (*-plase*) among other groups. Analogues of recombinant glycosylated proteins produced in different cell systems have been classified using Greek letters as indicators in the sequence of product introduction: erythropoietin (*epoetin alfa*, *beta* and so on) and glycoprotein hormones (*follitropin*) are examples. In the 1990s, a systematic scheme for naming monoclonal antibodies was implemented, based on the stem *-mab*, which indicates the origin (mouse, human, etc) of the antibody and its intended use: tumour, immunomodulator and so on.

As a result of the scientific and technical developments currently taking place, new products of biotechnology and other biological products are being introduced and more products can be expected for the treatment or prevention of disease. Examples of such new products include recombinant blood products, transgenic products (human proteins expressed in animals or plants), products for gene therapy and novel vaccines.

As this area is becoming more and more complex and challenging, the INN Expert Group has requested the WHO-INN Secretariat to prepare a working document intended to summarize and review the past and present INN situation in this field.

This document, first published on the website of the INN Programme in 2006, therefore presents an inventory of the policy decisions taken by the INN Expert Group during all these years of change, and of the names assigned to biological and biotechnological substances. Considering the potential for further developments in the field of biologicals, this review is intended to be a *living document* which will be regularly updated to include new policies, and future INNs assigned.

Comments and suggestions from all interested parties are most welcome and will be presented to the INN Expert Group for their consideration and for possible incorporation in future updates of this review.

You are reading the current updated version, also available as pdf-copy at:

http://www.who.int/medicines/services/inn/publication/en/index.html

1. PHARMACOLOGICAL CLASSIFICATION OF BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES [(1)]

Alimentary tract and metabolism

insulins (see item 4.16).

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antimicrobial, bactericidal permeability increasing polypeptides (see item 4.1).

Antineoplastics

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receptor molecules, native or modified (see item 4.26).

Hormones, hormone antagonists, hormone-release stimulating peptides or hormone-release inhibiting peptides (excluding insulins)

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growth hormone antagonists (see item 4.12)

oxytocin derivatives (see item 4.21)

pituitary / placental glycoprotein hormones (see item 4.24)

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synthetic polypeptides with a corticotropin-like action (see item 4.27)

vasoconstrictors, vasopressin derivatives (see item 4.30).

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antisense oligonucleotides (see item 4.2)

enzymes (see item 4.7)

gene therapy products (see item 4.9)

growth factors (see item 4.10)

peptides and glycopeptides (for special groups of peptides see -*actide* (see item 4.27), -*pressin* (see item 4.30), -*relin* (see item 4.25), -*tocin* (see item 4.21)) (see item 4.22).

2. CURRENT STATUS OF EXISTING STEMS OR SYSTEMS FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES[(1) (2) (3) (4) (5) (6) (7)]

2.1. Groups with respective stem

Name of the group	**Stem**
antisense oligonucleotides	*-rsen*
blood coagulation cascade inhibitors	*-cogin*
blood coagulation factors	*-cog*
colony stimulating factors	*-stim*
enzymes	*-ase*
erythropoietin type blood factors	*-poetin*
growth factors	*-ermin*
growth hormone derivatives	*som-*
heparin derivatives including low molecular mass heparins	*-parin*
hirudin derivatives	*-irudin*
pituitary hormone-release inhibiting peptides	*-relix*
interleukin receptor antagonists	*-kinra*
interleukin type substances	*-kin*
monoclonal antibodies	*-mab*
oxytocin derivatives	*-tocin*
peptides and glycopeptides (for special groups of peptides see *-actide*, *-pressin, -relin, -tocin*)	*-tide*
pituitary hormone-release stimulating peptides	*-relin*
receptor molecules, native or modified (a preceding infix should designate the target)	*-cept*
synthetic polypeptides with a corticotropin-like action	*-actide*
vasoconstrictors, vasopressin derivatives	*-pressin*

2.2. Groups with respective pre-stems

Name of the group	Pre-stem
antimicrobial, bactericidal permeability increasing polypeptides	*-ganan*
neurotrophins	*-neurin*

2.3. Groups with INN schemes

Name of the group
antithrombins
gene therapy products
insulins
interferons
pituitary / placental glycoprotein hormones

2.4. Groups without respective stems / pre-stems and without INN schemes

Name of the group
growth hormone antagonists
thrombomodulins
toxins

3. GENERAL POLICIES FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES

3.1. General policies for blood products [4]

- INNs have not been assigned to natural human blood products.
- Many natural blood products have well-established names, so the recombinant version should have a distinctive name reflecting as much as possible the established name used in the field.
- It is essential to add "activated" to the name of the blood product when this is presented for therapeutic use in its activated form.

3.2. General policies for fusion proteins[1] [4]

- INNs have been assigned to some fusion proteins. If a stem exists for one or the other part of the fusion protein, this stem should be brought into the name. This allows the constant part of a fusion protein to be recognized in the name.
- At present it is considered unnecessary to indicate that the product is a fusion product within the name, but this position may need to be reviewed in the future.

3.3. General policies for gene therapy products [2]

In 2005, the Nomenclature Scheme for Gene Therapy Products was formally adopted. The scheme is shown in Table 1.

[1] The list of INN for composite proteins published is given in Annex 1, including some fusion proteins

Table 1 Two-word scheme for gene therapy products

	prefix	infix	suffix
word 1 (gene component)	to contribute to the distinctive name e.g. *al-*; *bet-*; *val-*	to identify the gene using, when available, existing infixes for biological products or using similar infix as for the protein for which the gene codes. e.g. *-ermin-*: growth factor *-kin-*: interleukin *-lim-*: immunomodulator *-mul-*: multiple gene *-tusu-*: tumour suppression	*-(a vowel)gene* e.g. *-(o)gene*
word 2 (vector component)	to contribute to the distinctive name	e.g. *-adeno-*: adenovirus *-cana-*: canarypox virus *-herpa-*: herpes virus *-lenti-*: lentivirus *-morbilli-*: paramyxoviridae morbillivirus *-parvo-*: adeno-associated virus (parvoviridae dependovirus) *-retro-*: other retrovirus *-vaci-*: vaccinia virus	*-vec* (non-replicating viral vector) *-repvec* (replicating viral vector)
			-plasmid (plasmid vector)

In the case of non-plasmid naked DNA products, there is no need for a second word in the name.

3.4. General policies for glycosylated compounds [(8)]

For glycoproteins / glycopeptides

- For groups identified with a stem, e.g. for erythropoetins: *-poetin*, differences in the amino acid chain are indicated by using a random prefix and differences in the glycosylation pattern are indicated by another designator expressed by a Greek letter[2] spelt

[2] The transliteration of Greek letters in English, French and Spanish is given in Annex 2

in full and added as a second word to the name (e.g. *epoetin alfa (66)*, *darbepoetin alfa (85) see item 4.8*).

- For blood coagulation factors obtained by recombinant biotechnology, the differences in the glycosylation pattern are indicated by a Greek letter spelt in full and added as a second word to the name (e.g. *eptagog alfa (activated) (77), octocog alfa (73))*; when the amino acid sequence differs from the natural product this is indicated by using a random prefix (e.g. *beroctocog alfa (98)*); see item 4.5.

- Similarly, for enzymes identified with a stem *-ase* obtained by recombinant biotechnology and differing in the amino acid chain, these differences are indicated by using a random prefix and differences in the glycosylation pattern are indicated by a Greek letter spelt in full and added as a second word to the name (e.g. *alglucosidase alfa (91), bucelipase alfa (95))*; see item 4.7.

- The Greek letters should be used in the Greek alphabetical order (see Annex II).

3.5. General policies for immunoglobulins fractionated from plasma [(9) (10)]

Not to select an INN for immunoglobulins fractionated from plasma is the current policy.

The "systematic" or descriptive name is essential since the prescriber must know all the information conveyed by it and there is no benefit in assigning an INN from which it will not be readily apparent.

3.6. General policies for monoclonal antibodies [(1) (3) (11)3]

- INN for monoclonal antibodies (mAbs) are composed of a prefix, a substem A, a substem B and a suffix.
- The common stem for mAbs is *-mab,* placed as a suffix.
- The stem *-mab* is to be used for all products containing an immunoglobulin variable domain which binds to a defined target.

[3] It contains the revised naming scheme for monoclonal antibodies; the previous naming scheme for monoclonal antibodies is given in Annex 3

- Substem B indicates the species on which the immunoglobulin sequence of the mAb is based (shown in Table 2).

Table 2 Substem B for the species

a	rat
axo (pre-sub-stem)	rat/mouse
e	hamster
i	primate
o	mouse
u	human
xi	chimeric
-xizu-	chimeric-humanized
zu	humanized

The distinction between chimeric and humanized antibodies is as follows:

Chimeric: A chimeric antibody is one of which both chain types are chimeric as a result of antibody engineering. A chimeric chain is a chain that contains a foreign variable domain (V-D-J-REGION) (originating from one species other than human, or synthetic) linked to a constant region (C-REGION) of human origin.

Humanized: A humanized antibody is one of which both chain types are humanized as a result of antibody engineering. A humanized chain is a chain in which the complementarity determining regions (CDR) of the variable domains are foreign (originating from one species other than human, or synthetic) whereas the remaining chain is of human origin. By extension an antibody is described as humanized if more recent protocoles were used for the humanization.

The *–xizu-* infix is used for an antibody having both chimeric and humanized chains.
The *-axo-* infix is used for an antibody having both rat and mouse chains.

- Substem A indicates the target (molecule, cell, organ) class (shown in Table 3).

Table 3 Substem A for target class

-b(a)-	bacterial
-c(i)-	cardiovascular
-f(u)-	fungal
-k(i)-	interleukin
-l(i)-	immunomodulating
-n(e)- (under discussion	neural
-s(o)-	bone
-tox(a)-	toxin
-t(u)-	tumour
-v(i)-	viral

In principle, a single letter, e.g. *-b-* for bacterial is used as substem A. Whenever substem B starts with a consonant (e.g. x or z), to avoid problems in pronunciation, an additional vowel indicated in the table, e.g. *-ba-* is inserted.

Prefix

The prefix should be random i.e.. the only requirement is to contribute to a euphonious and distinctive name.

Second word

If the monoclonal antibody is conjugated to another protein or to a chemical (e.g. chelator), identification of this conjugate is accomplished by use of a separate, second word or acceptable chemical designation. For instance, for mAbs conjugated to a toxin, the suffix *-tox* is used in the second word.

If the monoclonal antibody is radiolabelled, the radioisotope is listed first in the INN, e.g. *technetium (^{99m}Tc) nofetumomab merpentan (81)*.

The prefix *peg-* can be used for pegylated mAbs, but this should be avoided if it leads to over-long INN. In most cases, it is best to adopt two-word INN for pegylated mAbs, with the first word describing the mAb and the second being *pegol* or a related designation.

3.7. General policies for non-glycosylated compounds [8]

For proteins / peptides:

- Identification of the group with a stem, e.g. for hirudin analogues:-*irudin*, and indication of differences in the amino acid chain by using a random prefix (e.g. *bivalirudin (72)*).
- Identification of the group with a word, e.g. insulin, and indication of differences in the composition of the amino acid chain as a second element of the name (e.g. *insulin argine (58)*).

3.8. General policies for skin substitutes [4]

The products within this system are made of cells within a matrix, and skin substitutes can be considered to be engineered tissue and thus fall outside the scope of the INN system.

3.9. General policies for transgenic products [4]

- If an INN already exists, the same name should be used for the transgenic product, qualified in some way to identify that this product is transgenic.
- A similar system to that used for glycosylated recombinant products is suggested to differentiate new or additional sources of the same substance, and the source of the substance should be included in the definition of the INN.

3.10. General policies for vaccines [4] [5] [6] [7]

- At present, vaccines are not included within the INN system, but names are assigned through recommendations of the Expert Committee on Biological Standardization and through the pharmacopoeial monograph.
- During the INN Consultation in 1993, it was agreed that the prerequisite for an INN application for a recombinant vaccine[4] would be fulfilled if the manufacturer was able to provide all

[4] The definition of recombinant vaccines is given in item 4.23

information outlined in the guidelines entitled Definition of INNs for Substances Prepared by Biotechnology (WHO / Pharm S / Nom 1348[(12)]).

- During the INN Consultation in 1998, following discussion on recombinant viruses, the experts agreed not to attempt to name live viruses.
- Another approach in vaccine technology seems to be the development of peptide vaccines[5] (epitopes involved in immune response formation): since these peptides are chemically well-defined, their naming will be less problematic.

[5] The definition of peptide vaccines is given in item 4.23

4. SUMMARY OF INN ASSIGNED TO BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES[(1) (3) (7) (8) (13) (14) (15) (16) (17) (18) (19) (20) (21)]

4.1. Antimicrobial, bactericidal permeability increasing polypeptides

The pre-stem for antimicrobial, bactericidal permeability increasing polypeptides is *-ganan*.

iseganan (85)[6], *omiganan (89), pexiganan (78)*.

4.2. Antisense oligonucleotides

The common stem for antisense oligonucleotides is *-rsen*.

afovirsen (97), *aganirsen (103)*, *alicaforsen (97)*, *anivamersen (105)*, *aprinocarsen (97)*, *beclanorsen (101)*, *cenersen (97)*, *custirsen (99)*, *eteplirsen (103), fomivirsen (97)*, *gataparsen (103)*, *mipomersen (100)*, *miravirsen (101)*, *oblimersen (97)*, *trabedersen (98)*, *trecovirsen (97)*.

4.3. Antithrombins

antithrombin III (60), *antithrombin alfa (93)* (Rec. Glycoprotein (432aa) from transgenic goats).

[6] The numbers in parentheses indicate the Proposed list number

4.4. Blood coagulation cascade inhibitors

The common stem for blood coagulation cascade inhibitors is *-cogin*.

drotrecogin alfa (activated) (86), *pegnivacogin (105)*, *taneptacogin alfa (90)*, *tifacogin (78)*.

4.5. Blood coagulation factors

The common stem for blood coagulation factors is *-cog*.

The sub-stems *-eptacog*, *-octocog* and *-nonacog*, have been selected up to date for recombinant blood coagulation factors.

A prefix will be necessary if the amino acid sequence does not match that of the naturally occurring material.

In accordance with the general policy, *alfa, beta,* etc, will be added for the glycoproteins (see item 3.4 - general policies for glycosylated compounds).

When the additional statement "activated" is needed, e.g. for the blood coagulation factor VIIa, it should be spelt out in full and added in parentheses after the name.

blood coagulation factor VII: *-eptacog*

eptacog alfa (activated) (77), *eptacog alfa pegol (activated) (101), vatreptacog alfa (activated) (98)*

blood factor VIII: *-octocog*

beroctocog alfa (98), *moroctocog alfa (72), octocog alfa (73)*, *simoctocog alfa (104), turoctocog alfa (104)*

blood factor IX: *-nonacog*

nonacog alfa (77), *nonacog beta pegol (104)*

blood coagulation factor XIII: *tridecacog*

catridecacog (99)

recombinant von Willebrand factor (vWF): -*vonicog*

vonicog alfa (102).

4.6. Colony stimulating factors

The common stem for colony stimulating factors is -*stim*.

ancestim (79) (cell growth factor), *garnocestim (86)* (immunomodulator), *pegacaristim (80)* (megakaryocyte growth factor), *romiplostim (97)* (thrombopoietin receptor (MPL) agonist)

combination of two different types of colony stimulating factors: -*distim*

leridistim (80), *milodistim (75)*

granulocyte colony stimulating factor (G-CSF) type substances: -*grastim*

filgrastim (64), *lenograstim (64)*, *lipegfilgrastim (105)*, *nartograstim (66)*, *pegfilgrastim (86)*, *pegnartograstim (80)*

granulocyte macrophage colony stimulating factor (GM-CSF) types substances: -*gramostim*

ecogramostim (62), *molgramostim (64)*, *regramostim (65)*, *sargramostim (66)*

macrophage stimulating factors (M-CSF) type substances: -*mostim*

cilmostim (71), *lanimostim (91)*, *mirimostim (65)*

interleukin-3 analogues and derivatives: -*plestim*

daniplestim (76), *muplestim (74)*.

4.7. Enzymes

The common stem for enzymes, in general, is -*ase*.

Sub-stems are referring to the activity of the substances.

proteinase:

with -ase suffix:
brinase (22), *calaspargase pegol (105)*, *kallidinogenase (22)*, *ocrase (28)*, *pegaspargase (64)*, *promelase (47)*, *rasburicase (82)*, *serrapeptase (31)*, *sfericase (40)*, *streptokinase (6)*, *urokinase (48)*, *urokinase alfa (77)*

without -*ase* suffix:
batroxobin (29), *bromelains (18)*, *chymopapain (26)*, *chymotrypsin (10)*, *defibrotide (44)*, *fibrinolysin (human) (10)*, *sutilains (18)*

Lipase*: -lipase*

bucelipase alfa (95), *rizolipase (22)*

enzymes with superoxide dismutase activity: *-dismase*

- *ledismase (70)*, *sudismase (58)*

- isomerase (belongs to this group but in which the preferred stem has not been used)

  orgotein (31), *pegorgotein (72)*

plasminogen activator combined with another enzyme: *-diplase*

amediplase (79)

tissue-type-plasminogen activators: *-teplase*

alteplase (73), *desmoteplase (80)*, *duteplase (62)*, *lanoteplase (76)*, *monteplase (72)*, *nateplase (73)*, *pamiteplase (78)*, *reteplase (69)*, *silteplase (65)*, *tenecteplase (7*9)

anistreplase (59) (belongs to this group but in which the preferred stem has not been used)

urokinase-type-plasminogen activators: *-uplase*

nasaruplase (76), *nasaruplase beta (86)*, *saruplase (76)*

others:

agalsidase alfa (84): human alpha-galactosidase isoenzyme A, isolated from human cell line, clone RAG 001, glycoform α

agalsidase beta (84): α-galactosidase (human clone λAG^{18} isoenzyme A subunit protein moiety reduced), glycoform β

alfimeprase (85): [3-L-serine]fibrolase-(3-203)-peptide (fibrolase : fibrinolytic enzyme isolated from *Agkistrodon contrix contrix* venom)

alglucerase (68): glucosylceramidase (human placenta isoenzyme protein moiety reduced)

alglucosidase alfa (91): human lysosomal prepro-α-glucosidase-(57-952)-peptide 199-arginine-223-histidine variant

asfotase alfa (104): tissue-nonspecific alkaline phosphatase- IgG_1 fusion protein;human tissue-nonspecific isozyme alkaline phosphatase (AP-TNAP, EC=3.1.3.1) fusion protein with leucyl-lysyl-human immunoglobulin G1 Fc region {(6-15)-H-CH2-CH3 of IGHG1*03} fusion protein with aspartyl-isoleucyl-deca(aspartic acid), dimer (493-493':496-496')-bisdisulfide

condoliase (102): endolyase, chondroitin ABC (C-ABC). glycosaminoglycan lyase chondroitin ABC endolyase 1 (chondroitinase ABC) *Proteus vulgaris*

dornase alfa (70): deoxyribonuclease (human clone 18-1 protein moiety)

epafipase (85): 2-acetyl-1-alkyl-*sn*-glycero-3-phosphocholine deacetylase-(6-400)-peptide(human)

eufauserase (84): broad spectrum serine-protease enzyme, extracted from the Antartic krill (*Euphausia superba*)

galsulfase (92): *N*-acetylgalactosamine 4-sulfatase (human CSL4S-342 cell)

glucarpidase (92): recombinant glutamate carboxypeptidase (carboxypeptidase G2)

hyalosidase (50): hyaluronoglucosaminidase *or* E.C. 3.2.1.35

hyaluronidase (1): enzymes of various origins which depolymerize hyaluronic acid

idursulfase (90): α-L-iduronate sulfate sulfatase

imiglucerase (72): 495-L-histidineglucosylceramidase (human placenta isoenzyme protein moiety)

laronidase (86): 8- L-histidine-α-L-iduronidase (human)

pegademase (63): adenosine deaminase, reaction product with succinic anhydride, esters with polyethylene glycol monomethyl ether
The source of the product should be indicated

pegloticase (98): tetramer α_4 of des-(1-5)-[6-threonine,45-threonine,290-lysine, 300-serine]uricase (EC 1.7.3.3, urate oxidase) from *Sus scrofa* (porcine), non acetylated, of which some of the lysine 6-amine residues are engaged in a carbamate linkage with a monomethylic ether of polyoxyethylene (macrogol)

pegadricase (105): pegylated Urate Oxidase from *Candida utilis*, [198-threonine(S>T)]uricase (EC 1.7.3.3, urate oxidase) *Pichia jadinii* (Yeast) (*Candida utilis*) tetramer, 6-amino group of an average of 3 lysine residues, mostly in position 16, 19, and 85 of each monomer, are amidified with α-(3-carboxypropanoyl)-ω-methoxypoly(oxyethylene)

penicillinase (10): an enzyme obtained by fermentation from cultures of *B.Cereus*

ranpirnase (81): ribonuclease (*Rana pipiens*)

streptodornase (6): enzyme obtained from cultures of various strains of Streptococcus hemolyticus and capable of hydrolysing desoxyribonucleoproteins

taliglucerase alfa (101): L-glutamyl-L-phenylalanyl-[495(*497*)- L-histidine(R>H)]human glucosylceramidase (beta-glucocerebrosidase) peptide with L-aspartyl-L-leucyl-L-leucyl-L-valyl-L-aspartyl-L-threonyl-L-methionine,glycosylated peptide *1-506*

tilactase (50): *β-D*-galactosidase *or* EC 3.2123

velaglucerase alfa (98): human glucosylceramidase (EC 3.2.1.45 or beta-glucocerebrosidase), glycoform α.

4.8. Erythropoietin type blood factors

The common stem for erythropoietin type blood factors is -*poetin*.

In the case of erythropoietins, it was decided to select *epoetin* together with a Greek letter to differentiate between compounds of the same amino acid sequence as human erythropoietin which vary in the glycosylation pattern (see item 3.4 - general policies for glycosylated compounds).

Substances with different amino acid sequences will be named using the -*poetin* stem and a random prefix.

darbepoetin alfa (85), *epoetin alfa (66)*, *epoetin beta (62)*, *epoetin gamma (67)*, *epoetin delta (85)*, *epoetin epsilon (72)*, *epoetin zeta (95)*, *epoetin theta (95)*, *epoetin kappa (97)*, *epoetin omega (73)*.

4.9. Gene therapy products

alferminogene tadenovec (95), *alipogene tiparvovec (99), amolimogene bepiplasmid (98)*, *beperminogene perplasmid (95)*, *contusugene ladenovec (97)*, *golnerminogene pradenovec (101)*, *riferminogene pecaplasmid (100)*, *sitimagene ceradenovec (97)*, *taberminogene vadenovec (100)*, *talimogene laherparepvec (104)*, *tipapkinogene sovacivec (102)*, *velimogene aliplasmid (97)*.

4.10. Growth factors

The common stem for growth factors is -*ermin*.

Sub-stems allow distinction between the various types of growth factors.

INNs for tumour necrosis factors (TNF) are also classified under the stem -*ermin*.

vascular endothelial growth factors: -*bermin*

telbermin (85)

epidermal growth factors: *-dermin*

murodermin (63), *nepidermin (97)*

fibroblast growth factors: *-fermin*

ersofermin (66), *palifermin (88)*, *repifermin (82)*, *sprifermin (105)*, *trafermin (74)*, *velafermin (94)*

leukaemia-*inhibiting* factors: *-filermin*

emfilermin (82)

tumour necrosis factors: *-nermin*

ardenermin (88), *dulanermin (99)*, *plusonermin (73)*, *sonermin (68)*, *tasonermin (78)*

platelet-derived growth factors: *-plermin*

becaplermin (74)

insulin-like growth factors: *-sermin*

mecasermin (66), *mecasermin rinfabate (92)*

transforming growth factors: *-termin*

cetermin (74), *liatermin (81)*

bone morphogenetic proteins: *-otermin*

avotermin (77), *dibotermin alfa (89)*, *eptotermin alfa (92)*, *radotermin (92)*

others:

dapiclermin (93) (modified ciliary neurotrophic factor (CNTF)).

4.11. Growth hormone (GH) derivatives

The common stem for growth hormone derivatives is *som-*.

human growth hormone derivatives:

somatrem (54), *somatropin (74), somatropin pegol (103)*

For substances other than human, suffixes are added to indicate the species specificity of the structure.

bovine-type substances: *-bove*

somagrebove (63), *somavubove (63)*, *sometribove (74)*, *somidobove (58)*

porcine-type substances: *-por*

somalapor (62), *somenopor (62)*, *somfasepor (66)*, *sometripor (75)*

salmon-type substances: *-salm*

somatosalm (69)

others (growth hormone related peptides):

somatorelin (57) (pituitary hormone-release stimulating peptides, see item 4.25), *somatostatin (46)* (growth hormone release inhibitor).

4.12. Growth hormone antagonists

pegvisomant (82).

4.13. Heparin derivatives including low molecular mass heparins

The common stem for heparin derivatives including low molecular mass heparins is *-parin*.

ardeparin sodium (68), *adomiparin sodium (104), bemiparin sodium (75)*, *certoparin sodium (70)*, *dalteparin sodium (77)*, *deligoparin sodium (89)*, *enoxaparin sodium (77)*, *heparin sodium (54)*, *livaraparin calcium (86)*,

minolteparin sodium (74), *nadroparin calcium (78)*, *parnaparin sodium (77)*, *reviparin sodium (78)*, *semuloparin sodium (99)*, *tafoxiparin sodium (102), tinzaparin sodium (77)*.

4.14. Hirudin derivatives

The common stem for hirudin derivatives is *-irudin*.

bivalirudin (72), *desirudin (76)*, *lepirudin (76)*, *pegmusirudin (77)*.

4.15. Pituitary hormone-release inhibiting peptides

The common stem for pituitary hormone-release inhibiting peptides is *-relix*.

abarelix (78), *cetrorelix (66)*, *degarelix (86)*, *detirelix (56)*, *ganirelix (65)*, *iturelix (79)*, *ozarelix (94)*, *prazarelix (81)*, *ramorelix (69)*, *teverelix (78)*.

4.16. Insulins

Up to now, the insulin derivatives have been named using the two-word approach. The compounds named represent a structure with an additional amino acid, such as *insulin argine (58)*, or represent modifications of the amino acid sequence, i.e. *insulin aspart (76)*.

biphasic insulin injection (16), *compound insulin zinc suspension (06)*, *dalanated insulin (104)*, *globin zinc insulin injection (06)*, *insulin argine (58)*, *insulin aspart (76)*, *insulin defalan (37)*, *insulin degludec (101)*, *insulin detemir (80)*, *insulin glargine (76)*, *insulin glulisine (84)*, *insulin human (48)*, *insulin lispro (72)*, *insulin tregopil (103), insulin zinc suspension (amorphous) (04)*, *insulin zinc suspension (crystalline) (04)*, *isophane insulin (04)*, *neutral insulin injection (15)*, *protamine zinc insulin injection (06)*

argine: B30-yl-L-arginyl-L-arginine

aspart: [B28-L-aspartic acid]

dalanated: des-B30-alanine

defalan: des-B1-phenylalanine

degludec: $N^{6,\ B29}$-[*N*-(15-carboxypentadecanoyl)-L-γ-glutamyl]-des-30B-L-threonine

detemir: $N^{6,B29}$-tetradecanoyl-des-B30-L-threonine

glargine: [A21-glycine], B30-yl-L-arginyl-L-arginine

glulisine: [B3-lysine, B29-glutamic acid]

lispro: [B28-L-lysine, B29-L-proline]

tregopil: $N^{6,\ B29}$-(4,7,10,13-tetraoxatetradecanoyl).

4.17. Interferons

Interferon was published as an INN in 1962 with a general definition based on the origin and activity, e.g. "a protein formed by the interaction of animal cells with viruses capable of conferring on animal cells resistance to virus infection".

The name was revised in the 1980s when human interferon and its variations *alfa*, *beta* and *gamma* were produced by recombinant biotechnology. The INN Expert Group would have preferred to replace the old INN interferon by alfaferon, betaferon and gammaferon; however, this approach could not be adopted as these names had already been registered as trade marks. The system adopted was thus to take interferon alfa, interferon beta and interferon gamma, and to provide, when necessary, for further distinction by additional numbers, or in the case of mixtures, by additional codes. Additional Arabic numbers can be used to distinguish subspecies which differ significantly in primary amino acid sequence, but are still considered to belong to one of the primary groups e.g. Interferon alfa-1, interferon alfa- 2. Small (lower case) letters are used to subdivide such groups further on the basis of less significant differences like one, two or three amino acid differences or post translational modifications, including glycosylation e.g. Interferon alfa-2a, Interferon alfa-2b, Interferon beta-1a, Interferon beta-1b.

albinterferon alfa-2b (99), *cepeginterferon alfa-2b (105), interferon alfa (73)*, *interferon alfacon-1 (77)*, *interferon beta (73)*, *interferon gamma (73)*, *peginterferon alfa-2a (84)*, *peginterferon alfa-2b (84)*, *peginterferon lambda-1a (105)*.

4.18. Interleukin receptor antagonists

The common stem for interleukin receptor antagonists is *-kinra*.

interleukin-1 (IL-1) receptor antagonists: *-nakinra*

anakinra (72)

interleukin-4 (IL-4) receptor antagonists: *-trakinra*

pitrakinra (87).

4.19. Interleukin type substances

The common stem for interleukin type substances is *-kin*.

In accordance with general policy for naming glycosylated proteins (see item 3.4), it was agreed to publish the INNs for glycosylated interleukins with alfa, beta.

interleukin-1 (IL-1) analogues and derivatives: *-nakin*

interleukin-1α analogues and derivatives: *-onakin*

pifonakin (77)

interleukin-1β analogues and derivatives: *-benakin*

mobenakin (72)

interleukin-2 (IL-2) analogues and derivatives: *-leukin*

adargileukin alfa (89), *aldesleukin (63)*, *celmoleukin (65)*, *denileukin diftitox (78)*, *pegaldesleukin (74)*, *teceleukin (67)*, *tucotuzumab celmoleukin (95)*

interleukin-3 (IL-3) analogues and derivatives: -*plestim* (belongs to this group but in which the preferred stem has not been used)

daniplestim (76), *muplestim (74)*

interleukin-4 (IL-4) analogues and derivatives: -*trakin*

binetrakin (82)

interleukin-6 (IL-6) analogues and derivatives: -*exakin*

atexakin alfa (72)

interleukin-8 (IL-8) analogues and derivatives: -*octakin*

emoctakin (74)

interleukin-10 (IL-10) analogues and derivatives: -*decakin*

ilodecakin (81)

interleukin-11 (IL-11) analogues and derivatives: -*elvekin*

oprelvekin (76)

interleukin-12 (IL-12) analogues and derivatives: -*dodekin*

edodekin alfa (79)

interleukin-13 (IL-13) analogues and derivatives: -*tredekin*

cintredekin besudotox (92)

a recombinant human interleukin-18 (IL-18) with 157 amino acids:

iboctadekin (92)

a recombinant human interleukin-21: -*enicokin*

denenicokin (99)

neurotrophins (interleukin-78, brain derived neurotropic factor): -*neurin* (pre-stem)

abrineurin (84).

4.20. Monoclonal antibodies

The common stem for monoclonal antibodies is *-mab*.

INNs for monoclonal antibodies alphabetically by origin:

***-axomab* (pre-sub-stem, rat-murine hybrid)**

catumaxomab (93), *ertumaxomab (93)*

***-omab* (mouse origin)**

abagovomab (95), *afelimomab (80)*, *altumomab (80)*, *anatumomab mafenatox (86), arcitumomab (74)*, *bectumomab (81)*, *besilesomab (92)*, *biciromab (66)*, *blinatumomab (100)*, *capromab (80)*, *detumomab (80)*, *dorlimomab aritox (66)*, *edobacomab (80)*, *edrecolomab (74)*, *elsilimomab (89)*, *enlimomab (80)*, *enlimomab pegol (77)*, *epitumomab (97)*, *epitumomab cituxetan (89)*, *faralimomab (81)*, *gavilimomab (84)*, *ibritumomab tiuxetan (86)*, *igovomab (86)*, *imciromab (66)*, *inolimomab (80)*, *lemalesomab (86)*, *maslimomab (66)*, *minretumomab (80)*, *mitumomab (82)*, *moxetumomab pasudotox (102)*, *nacolomab tafenatox (80)*, *naptumomab estafenatox (96)*, *nerelimomab (81)*, *odulimomab (81)*, *oregovomab (86)*, *racotumomab (100)*, *satumomab (81)*, *sulesomab (86)*, *taplitumomab paptox (84)*, *technetium (^{99m}Tc) fanolesomab (86)*, *technetium (^{99m}Tc) nofetumomab merpentan (81)*, *technetium (^{99m}Tc) pintumomab (86)*, *telimomab aritox (66)*, *tenatumomab (99)*, *tositumomab (80)*, *vepalimomab (80)*, *zolimomab aritox (80)*

***-umab* (human origin)**

adalimumab (85), *adecatumumab (90)*, *atinumab (104), atorolimumab (80)*, *belimumab (89)*, *bertilimumab (88)*, *briakinumab (101)*, *brodalumab (105)*, *canakinumab (97), carlumab (104), cixutumumab (100)*, *conatumumab (99), daratumumab (101), denosumab (94)*, *drozitumab (103), efungumab (95)*, *exbivirumab (91)*, *fezakinumab (101)*, *figitumumab (100)*, *foralumab (103)*, *foravirumab (100)*, *fresolimumab (101), fulranumab (104)*, *ganitumab (103), gantenerumab (97), glembatumumab (102)*, *golimumab (91)*, *icrucumab (104)*, *intetumumab (101)*, *ipilimumab (94)*, *iratumumab (94)*, *lerdelimumab (86)*, *lexatumumab (95)*, *libivirumab (91)*, *lucatumumab (98), mapatumumab (93)*, *mavrilimumab (102)*, *metelimumab (88)*, *morolimumab (79)*, *namilumab (104)*, *narnatumab (105)*, *nebacumab (66)*, *necitumumab (100)*, *ofatumumab (93)*, *olaratumab (103), oxelumab (105)*, *panitumumab (96)*, *panobacumab (100), pritumumab (89)*, *radretumab (104), rafivirumab (100)*, *ramucirumab (100)*, *raxibacumab (92)*, *regavirumab (80)*, *rilotumumab (101)*, *robatumumab (100)*, *roledumab (103)*, *secukinumab (102)*, *sevirumab (66)*, *sifalimumab (104)*, *sirukumab (105)*, *stamulumab*

(95), *tabalumab (105)*, *teprotumumab (101)*, *tralokinumab (102),* *tremelimumab (97)*, *tuvirumab (66)*, *urelumab (104), ustekinumab (99)*, *vesencumab (104), votumumab (80)*, *zalutumumab (93)*, *zanolimumab (92)*, *ziralimumab (84)*

-*ximab* (chimeric origin)

abciximab (80), *amatuximab (104)*, *basiliximab (81)*, *bavituximab (95)*, *brentuximab vedotin (103)*, *cetuximab (82)*, *clenoliximab (77)*, *ecromeximab (87)*, *ensituximab (103)*, *galiximab (89)*, *girentuximab (101)*, *indatuximab ravtansine (105)*, *infliximab (77)*, *iodine (^{124}I) girentuximab (101)*, *keliximab (81)*, *lumiliximab (90)*, *pagibaximab (93)*, *priliximab (80)*, *rituximab (77)*, *siltuximab (100)*, *teneliximab (87)*, *ublituximab (104),* *vapaliximab (87)*, *volociximab (93)*

-*xizumab* (chimeric/humanized origin)

otelixizumab (99)

-*zumab* (humanized origin)

alacizumab pegol (98), alemtuzumab (83), *anrukinzumab (98), apolizumab (87)*, *aselizumab (88)*, *bapineuzumab (93)*, *benralizumab (102)*, *bevacizumab (86)*, *bivatuzumab (86)*, *blosozumab (105), cantuzumab mertansine (105)*, *cantuzumab ravtansine (105)*, *cedelizumab (81)*, *certolizumab pegol (97)*, *citatuzumab bogatox (99), yttrium (^{90}Y)* *clivatuzumab tetraxetan (102), crenezumab (105), dacetuzumab (98),* *daclizumab (78)*, *dalotuzumab (10)*, *eculizumab (87)*, *efalizumab (85),* *elotuzumab (100)*, *enavatuzumab (104)*, *enokizumab (104), epratuzumab (82)*, *erlizumab (84)*, *etaracizumab (99)*, *etrolizumab (104)*, *farletuzumab (100)*, *felvizumab (77)*, *fontolizumab (87)*, *gemtuzumab (83)*, *gevokizumab (104), ficlatuzumab (105)*, *ibalizumab (97)*, *inotuzumab ozogamicin (92)*, *itolizumab (103), ixekizumab (105)*, *labetuzumab (85)*, *lebrikizumab (101)*, *lintuzumab (86)*, *lorvotuzumab mertansine (103), matuzumab (88)*, *mepolizumab (81)*, *milatuzumab (98), mogamulizumab (104)*, *motavizumab (95)*, *natalizumab (79)*, *nimotuzumab (94)*, *obinutuzumab (101)*, *ocrelizumab (95)*, *olokizumab (103)*, *omalizumab (84)*, *onartuzumab (104)*, *oportuzumab monatox (100)*, *ozoralizumab (105)*, *palivizumab (79)*, *pascolizumab (87)*, *pateclizumab (105)*, *pertuzumab (89)*, *pexelizumab (86)*, *ponezumab (104)*, *ranibizumab (90)*, *reslizumab (85)*, *rontalizumab (101)*, *rovelizumab (81)*, *ruplizumab (83)*, *samalizumab (105)*, *sibrotuzumab (86)*, *siplizumab (87)*, *solanezumab (100)*, *sontuzumab (94)*, *suvizumab (102),* *tadocizumab (94)*, *talizumab (89)*, *tanezumab (99)*, *tefibazumab (92)*, *teplizumab (97), tigatuzumab (98), tocilizumab (90)*, *toralizumab (87)*, *trastuzumab (78)*, *trastuzumab emtansine (103)*, *tregalizumab (104)*, *tucotuzumab celmoleukin (95)*, *urtoxazumab (90)*, *vatelizumab (105),*

vedolizumab (100), *veltuzumab (98)*, *visilizumab (84)*, *yttrium* ^{90}Y *tacatuzumab tetraxetan (93)*

***Others*:** *muromonab-CD3 (59)* (the first monoclonal antibody to which an INN was assigned belongs to this group but it was named before the stem was established).

4.21. Oxytocin derivatives

The common stem for oxytocin derivatives is *-tocin*.

argiprestocin (13), *aspartocin (11)*, *carbetocin (45)*, *cargutocin (35)*, *demoxytocin (22)*, *nacartocin (51)*, *oxytocin (13)*.

4.22. Peptides and glycopeptides

for special groups of peptides see *-actide* (see item 4.27), *-pressin* (see item 4.30), *-relin* (see item 4.25), *-tocin* (see item 4.21)

The common stem for peptides and glycopeptides is *-tide*.

analgesic: *leconotide (86)*, *ziconotide (78)*

angiogenesis inhibitor: *cilengitide (81)*

angiotensin converting-enzyme inhibitor: *teprotide (36)*

antianaemic: *peginesatide (103)*

anti-inflammatory: *icrocaptide (89)*

antiarrythmic: *danegaptide (101)*, *rotigaptide (94)*

antidepressant: *nemifitide (87)*

antidiabetic: *amlintide (76)*, *davalintide (101)*, *exenatide (89)*, *lixisenatide (99)*, *pramlintide (74)*, *seglitide (57)*

antidiarrhoeal: *lagatide (75)*

antithrombotic: *eptifibatide (78)* (*-fiba-* is a pre-substem for platelet aggregation inhibitor (GPIIb/IIIa receptor antagonist))

antiviral: *enfuvirtide (85)*, *tifuvirtide (91)*

atrial natriuretic factor type substance: *anaritide (57)*, *cenderitide (105), neseritide (80)*, *ularitide (69)*

autoimmune disorders: *dirucotide (100)*

cardiac stimulant: *carperitide (65)*

diagnostic: *betiatide (58)*, *bibapcitide (78)*, *ceruletide (34)*, *depreotide (80)*, *fluciclatide (^{18}F) (103)*, *maraciclatide (103)*, *mertiatide (60)*, *pendetide (70)*, *technetium (^{99m}Tc) apcitide (86)*, *teriparatide (50)*

expectorant (in cystic fibrosis): *lancovutide (99)*

gastro-intestinal bleeding / antineoplastic: *edotreotide (84)*, *ilatreotide (68)*, *lanreotide (64)*, *octreotide (52)*, *pentetreotide (66)*, *vapreotide (62)*

gastro-intestinal functions normalizing agent: *linaclotide (97)*, *plecanatide (104)*

glucagon-like peptide (GLP) analogues: *-glutide*

albiglutide (97), *dulaglutide (103)*, *elsiglutide (104), liraglutide (87)*, *semaglutide (101)*, *taspoglutide (99)*, *teduglutide (90)*

growth stimulant-veterinary: *nosiheptide (35)*

gut motility increasing: *ociltide (52)*

hormone analogue: *semparatide (80)*

immunological agents - antineoplastics: *almurtide (74)*, *delmitide (92)*, *edratide (89)*, *goralatide (72)*, *mifamurtide (95)*, *murabutide (49)*, *pentigetide (60)*, *pimelautide (53)*, *prezatide copper acetate (67)*, *rolipoltide (94)*, *romurtide (61)*, *tabilautide (60)*, *temurtide (60)*, *tigapotide (95)*

immunological agents for active immunization: *-motide* (see item 4.23)

amilomotide (105), *disomotide (94)*, *elpamotide (103), ovemotide (94)*, *tertomotide (98), tiplimotide (82)*

inhibition of growth hormone release: *pasireotide (90)*

kallicrein inhibitor: *ecallantide (93)*

melanocortin receptor agonist: *afamelanotide (99)*, *bremelanotide (95)*,

neuromodulator / neuroprotective agent: *davunetide (100)*, *ebiratide (56)*, *obinepitide (96)*, *vanutide cridificar (100)*

peptic ulcer: *sulglicotide (29)*, *triletide (50)*

pulmonary surfactant: *lusupultide (80)*, *sinapultide (78)*

sedative: *emideltide (70)*

thrombin receptor as an agonist, promoter of bone and skin wound healing: *rusalatide (96)*

transforming growth factor beta-1 inhibitor: *disitertide (99)*

treatment of Parkinson's disease: *doreptide (59)*, *pareptide (38)*

zonulin antagonist (in celiac disease): *larazotide (99)*

other: *defibrotide (44)* (nucleotide).

4.23. Peptide vaccines / recombinant vaccines

Definition of peptide vaccines: vaccine in which antigens are produced from synthetic peptides and transported through the bloodstream by an adjuvant, in order to stimulate an immune response.

Definition of recombinant vaccines: vaccine produced from a cloned gene.

Description of recombinant vaccines: there are certain antigens on viruses and bacteria which are better at stimulating an antibody response by the animal than others. The genes for these antigens can be isolated, and made to produce large quantities of the antigens they code for. A recombinant

vaccine contains these antigens, not the whole organism. Compare with "modified live vaccine" and "killed vaccine".

The following substances are peptide vaccines (see item 4.22): *-motide amilomotide (105)*, *disomotide (94)*, *elpamotide (103)*, *ovemotide (94)*, *tertomotide (98)*, *tiplimotide(82)*.

The following substance is the recombinant vaccine:

verpasep caltespen (95) (heat-shock protein HSP 65 (*Mycobacterium bovis* strain BCG) fusion protein with transcription factor E7 (human papilloma virus 16)).

The suffix *-tespen* is the indicator of heat shock protein.

4.24. Pituitary / placental glycoprotein hormones

The names selected by the International Union of Pure and Applied Chemistry–International Union of Biochemistry (IUPAC-IUB) have, to date, been chosen for compounds with an amino acid sequence identical to that of the naturally occurring human hormones. Addition of a Greek letter as the second part of the name will allow differentiation of different glycosylation patterns for compounds produced by biotechnology (see item 3.4 - general policies for glycosylated compounds).

follicle stimulating hormones: ending in *(-)follitropin*

corifollitropin alfa (80), *follitropin alfa (71)*, *follitropin beta (75)*, *urofollitropin (57)*, *varfollitropin alfa (101)*

gonadotropin: ending in *-gonadotropin*

choriogonadotropin alfa (76), *chorionic gonadotrophin (01)*: chorionic gonadotropins, obtained from human serum and urine during pregnancy and has both lutropin and follitropin activity

serum gonadotrophin (01): used for the follicle stimulating hormone (FSH, follitropin) from serum of pregnant mares

luteinizing hormones: ending in *(-)lutropin*

lutropin alfa (71).

4.25. Pituitary hormone-release stimulating peptides

The common stem for pituitary hormone-release stimulating peptides is *-relin.*

LHRH-release-stimulating peptides:

avorelin (74), *buserelin (36)*, *deslorelin (61)*, *fertirelin (42)*, *gonadorelin (32)*, *goserelin (55)*, *histrelin (53)*, *leuprorelin (47)*, *lutrelin (51)*, *nafarelin (50)*, *peforelin (93)*, *triptorelin (58)*

growth hormone release-stimulating peptides: *-morelin*

anamorelin (97), *capromorelin (83)*, *dumorelin (59)*, *examorelin (72)*, *ipamorelin (78)*, *lenomorelin (105), macimorelin (100)*, *pralmorelin (77)*, *rismorelin (74)*, *sermorelin (56)*, *somatorelin (57)*, *tabimorelin (86)*, *tesamorelin (96), ulimorelin (103)*

thyrotropin releasing hormone analogues: *-tirelin*

azetirelin (60), montirelin (58), orotirelin (58), *posatirelin (60)*, *protirelin (31)*, *taltirelin (75)*

thyrotropin alfa (78) (thyrotropin releasing hormone (TRH) analog, belongs to this group but in which the preferred stem has not been used)

other: *corticorelin (66)* (diagnostic agent).

4.26. Receptor molecules, native or modified

The stem for receptor molecules, native or modified is *-cept.*

A preceding infix should designate the target.

B-cell activating factor receptors: *-ba-*
briobacept (98)

vascular endothelial growth factor receptors: *-ber-*
aflibercept (96), conbercept (105)

complement receptors: *-co-*
mirococept (91)

subgroup of interferon receptors: *-far-*
bifarcept (86)

lymphocyte function-associated antigen 3 receptors: *-lefa-*
alefacept (84)

interleukin-1 receptors: *-na-*
rilonacept (95)

tumour necrosis factor receptors: *-nercept*.
baminercept (99), etanercept (81), *lenercept (72)*, *onercept (86)*, *pegsunercept (95)*

cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) receptors: *-ta-*
abatacept (91), belatacept (93)

transmembrane activator and calcium modulator and cyclophilin ligand interactor: *-taci-*
atacicept (95)

transforming growth factor receptors: *-ter-*
dalantercept (105), *sotatercept (104)*

antiviral receptors: *-vir-*
alvircept sudotox (69).

4.27. Synthetic polypeptides with a corticotropin-like action

The common stem for synthetic polypeptides with a corticotropin-like action is *-actide*.

alsactide (45), codactide (24), giractide (29), norleusactide (18), seractide (31), tetracosactide (18), tosactide (24), tricosactide (44), tridecactide (97).

4.28. Thrombomodulins

sothrombomodulin alfa (101), thrombomodulin alfa (94).

4.29. Toxins

toxin ML-1 (mistletoe lectin I) *(Viscum album)*: *aviscumine (86)*.

4.30. Vasoconstrictors, vasopressin derivatives

The common stem for vasoconstrictors, vasopressin derivatives is *-pressin*.

argipressin (13), *desmopressin (33)*, *felypressin (13)*, *lypressin (13)*, *ornipressin (22)*, *selepressin (105)*, *terlipressin (46)*, *vasopressin injection (16)*.

4.31. Various

- *alisporivir (100)*: [8-(*N*-methyl-D-alanine),9-(*N*-ethyl-L-valine)]cyclosporine

- *agatolimod (98)*: DNA, d(*P*-thio)(T-C-G-T-C-G-T-T-T-T-G-T-C-G-T-T-T-T-G-T-C-G-T-T)

- *angiotensin II (65)*: 5-L-isoleucineangiotensin II (the source of the material should be *indicated*)

- *angiotensinamide (12)*: N-{1-{N-{N-{N-[N-(N^2-asparaginylarginyl)valyl]tyrosyl}valyl}histidyl}prolyl}-3-phenylalanine

- *bevasiranib (99)*: siRNA inhibitor of Vascular Endothelial Growth Factor (VEGF) production

- *calcitonin (80)*: a polypeptide hormone that lowers the calcium concentration in blood (the species specificity should be indicated in brackets behind the name)

- *conestat alfa (98)*: human plasma protease C1 inhibitor (C1 esterase inhibitor) (*N*,*O*-glycosylated recombinant protein expressed in the mammary gland of transgenic rabbits), glycoform α

- *delcasertib (105)*: human immunodeficiency virus 1 protein Tat-(46-57)-peptide (1→1')-disulfide with L-cysteinyl-[mouse protein kinase C delta type-(8-17)-peptide]

- *epelestat (92)*: human recombinant neutrophil elastase inhibitor, bovine pancreatic trypsin inhibitor (BPTI) homologue

- *edifoligide (89)*: oligonucleotide

- *egaptivon pegol (104)*: a pegylated aptamer which binds von Willebrand factor; 5'-*O*-{[6-(carboxyamino)hexyl]hydroxyphosphoryl}-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyadenylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-*O*-methyl-*P*-thioguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-2'-deoxyguanylyl-(3'→5')-thymidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methyluridylyl-(3'→5')-2'-deoxycytidylyl-(3'→5')-2'-*O*-methyladenylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→5')-2'-*O*-methylguanylyl-(3'→5')-2'-*O*-methylcytidylyl-(3'→3')-thymidine, carbamate ester with monomethyl ether of polyethylene gycol (20 kDa)

- *hemoglobin glutamer (80)*: the species specificity should be indicated in brackets behind the name, "(bovine)"; the average mass of the polymer is given as e.g. haemoglobin glutamer-250 for 250kD

- *hemoglobin crosfumaril (76)*: hemoglobin A_0 (human $\alpha_2\beta_2$ tetrameric subunit), α-chain 99,99'-diamide with fumaric acid

- *hemoglobin raffimer (89)*

- *imetelstat (101)*: oligonucleotide telomerase inhibitor; 3'-amino-3'-deoxy-*P*-thiothymidylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioadenylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioguanylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioguanylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioguanylyl-(3'→5')-3'-amino-3'-deoxy-*P*-thiothymidylyl-(3'→5')-3'-amino-3'-deoxy-*P*-thiothymidylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioadenylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioguanylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioadenylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thiocytidylyl-(3'→5')-3'-amino-2',3'-dideoxy-*P*-thioadenylyl-(3'→5')-3'-amino-2',3'-dideoxyadenosine 5'-{*O*-[2-hydroxy-3-(hexadecanoylamino)propyl] hydrogen phosphorothioate}

- *iodinated (^{125}I) human serum albumin (24)*: human serum albumin iodinated with radioactive iodine (^{125}I)

- *iodinated (^{131}I) human serum albumin (24)*: human serum albumin iodinated with radioactive iodine (^{131}I)

- *iroplact (74)*: *N*-L-methionyl blood platelet factor 4 (human subunit)

- *ismomultin alfa (91)*: 47-261-Glycoprotein gp 39 (human clone CDM8-gp39 reduced)

- *litenimod (96)*: (3'-5')d(*P*-thio)(T-A-A-A-C-G-T-T-A-T-A-A-C-G-T-T-A-T-G-A-C-G-T-C-A-T)

- *macrosalb (^{131}I) (33)*: macroaggregated iodinated (^{131}I) human albumin

- *macrosalb (^{99m}Tc)(33)*: technetium (^{99m}Tc) labelled macroaggregated human serum albumin

- *metenkefalin (97)*: L-tyrosylglycylglycyl-L-phenylalanyl-L-methionine β-endorphin human-(1-5)-peptide

- *metreleptin (82)*: *N*-methionylleptin (human)

- *mirostipen (85)*: [23-methionine] human myeloid progenitor inhibitory factor 1-(23-99)-peptide

- *nagrestipen (76)*: 26-L-alaninelymphokine MIP 1α (human clone pAT464 macrophage inflammatory)

- *ocriplasmin (101)*: truncated human plasmin:
human plasmin heavy chain A-(543-561)-peptide (548-666;558-566)-bisdisulfide with human plasmin light chain B

- *opebacan (83)*: 132-L-alanine-1-193-bactericidal / permeability-increasing protein (human)

- *orgotein (31)*: a group of soluble metalloproteins isolated from liver, red blood cells, and other mammalian tissues

- *ovandrotone albumin (52)*: 3-[(3,17-dioxoandrost-4-en-7α-yl)thio]propionic acid, serum albumin conjugate

- *parathyroid hormone (90)*: non glycosylated human parathyroid hormone, the origin should be indicated between brackets after the INN, for example (r. *E. coli*) for recombinant produced by *Escherichia coli*

- *pegaptanib (88)*: 5'-ester of (2'-deoxy-2'-fluoro)C-Gm-Gm-A-A-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)C-Am-Gm-(2'-deoxy-2'-fluoro)U-Gm-Am-Am-(2'-deoxy-2'-fluoro)U-Gm-(2'-deoxy-2'-fluoro)C-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)U-Am-(2'-deoxy-2'-fluoro)U-Am-(2'-deoxy-2'-fluoro)C-Am-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)C-(2'-deoxy-2'-fluoro)C-Gm-(3'→3')-dT with α,α'-[[(1*S*)-1-[[5-(phosphonooxy)pentyl]carbamoyl]pentane-1,5-diyl]bis(iminocarbonyl)]bis[ω-methoxypoly(oxyethane-1,2-diyl)]

- *pegdinetanib (103)*: 94 residues protein derived from human fibronectin 10th type III domain, pegylated:
glycyl[1438-L-arginine(D>R),1439-L-histidine(A>H),1441-L-histidine(A>H),1442-L-phenylalanine(V>F),1443-L-proline(T>P),1444-L-threonine(V>T),1467-L-leucine(G>L),1468-L-glutamine(S>Q),1469-L-proline(K>P),1470-L-proline(S>P),1492-L-aspartic acid(G>D),1493-glycine(R>G),1494-L-arginine(G>R),1495-L-asparagine(D>N),1496-glycine(S>G),1497-L-arginine(P>R),1498-L-leucine(A>L),1499-L-leucine(S>L),1501-L-isoleucine(K>I),1515-*S*-[(3*RS*)-1-(1-{[α-

methylpoly(oxyethylene)]carbamoyl}-3-[({[α-methylpoly(oxyethylene)]carbamoyl}oxy)methyl]-8,13-dioxo-1,4-dioxa-9,12-diazapentadecan-15-yl)-2,5-dioxopyrrolidin-3-yl]-L-cysteine(S>C)]human fibronectin-(1424-1516)-peptide

- *rintatolimod (102)*: poly[5']-inosinylyl-(3'→) duplex with poly[dodecakis[3']-cytidylyl-(5'→)3')-uridylyl-(5'→)

- *secretin (01)*: hormone of the duodenal mucosa which activates the pancreatic secretion and lowers the blood-sugar level

- *serelaxin (105)*: human relaxin 2 (relaxin H2)

- *talactoferrin alfa (93)*: recombinant human lactoferrin

- *tadekinig alfa (90)*: interleukin-18 binding protein (human gene IL 18BP isoform a precursor)

- *thrombin alfa (97)*: human thrombin (recombinant, glycoform α)

- *tiprelestat (103)*: human elafin (elastase-specific inhibitor, skin-derived antileukoproteinase, peptidase inhibitor 3)

- *torapsel (91)*: 42-89-glycoprotein (human clone PMT21:PL85 P-selectin glycoprotein ligand 1) fusion protein with immunoglobulin (human constant region)

- *tremacamra (78)*: 1-453-glycoprotein ICAM-I (human reduced)

- *troplasminogen alfa (99)*: thrombin-activable plasminogen; endo-[(558a(*559*)-558h(*365*))-human coagulation factor XI-(363-370)-peptide]-des-(559-562)-[606(*610*)-lysine,623(*627*)-lysine]human plasminogen, glycoform α

- *votucalis (96)*: methionyl[145-leucine]FS-HBP2 (*Rhipicephalus appendiculatus* (Brown ear tick) Female-Specific Histamine-Binding Protein 2).

5. CURRENT CHALLENGES

The challenges currently faced include the following:

- The INN Expert Group, when selecting names for recombinant proteins, has to deal not with substances with well-defined structures but with products of highly complex composition or even with mixtures of such products.
- It is not only modified proteins that might differ from their naturally occurring counterparts, products derived by expression of the natural gene in foreign host cells may also differ structurally, biologically or immunologically from the natural protein.
- Glycoproteins particularly may occur in forms that differ in the structure of one or more of their carbohydrate units, a phenomenon known as microheterogeneity and resulting in a heterogeneous population of molecules. Such differences may affect both the size and the charge of individual glycoproteins.
- A variety of novel biotechnology-derived products are under development, all of which will require specific policies on how to deal with such products.
- Clearly, the INN nomenclature of biological medicinal products is an area of increasing complexity.

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** These documents are available on the INN Programme Website at: http://www.who.int/medicines/services/inn/en/*

ANNEX 1

The list of INN for composite proteins published[7]

classified by groups

-ase

asfotase alfa *(104)*

tissue-nonspecific alkaline phosphatase- IgG_1 fusion protein;human tissue-nonspecific isozyme alkaline phosphatase (AP-TNAP, EC=3.1.3.1) fusion protein with leucyl-lysyl-human immunoglobulin G1 Fc region {(6-15)-H-CH2-CH3 of IGHG1*03} fusion protein with aspartyl-isoleucyl-deca(aspartic acid), dimer (493-493':496-496')-bisdisulfide

-cept

abatacept *(91)*

1-25-oncostatin M (human precursor) fusion protein with CTLA-4 (antigen) (human) fusion protein with immunoglobulin G1 (human heavy chain fragment), bimolecular (146→146')-disulfide

aflibercept *(96)*

des-432-lysine-[human vascular endothelial growth factor receptor 1-(103-204)-peptide (containing Ig like C2 type 2 domain) fusion protein with human vascular endothelial growth factor receptor 2-(206-308)-peptide (containing Ig like C2 type 3 domain fragment) fusion protein with human immunoglobulin G1-(227 *C*-terminal residues)-peptide (Fc fragment)], (211-211':214-214')-bisdisulfide dimer

atacicept *(95)*

[86-serine,101-glutamic acid,196-serine,197-serine,222-aspartic acid,224-leucine][human tumor necrosis factor receptor superfamily member 13B-(30-

[7] It should be noted that this list may not be comprehensive and the descriptions under the names are the ones published

110)-peptide (TACI fragment containing TNFR-Cys 1 and TNFR-Cys 2) fusion protein with human immunogobulin G1-(232 *C*-terminal residues)-peptide (γ1-chain Fc fragment), (92-92':95-95')-bisdisulfide dimer

baminercept *(99)*

human tumor necrosis factor receptor superfamily member 3 (lymphotoxin-β receptor, TNF C receptor)-(2-195)-peptide (fragment of extracellular domain) fusion protein with human immunoglobulin heavy constant γ1 chain Fc fragment [227 residues, hinge (195-205) des-(1-4),C5>V, CH2 (206-315), CH3 (316-421) des-K^{107}]

conbercept *(105)*

fusion protein for immune applications (FPIA) comprising *Homo sapiens* FLT1 (fms-related tyrosine kinase 1, vascular endothelial growth factor receptor 1, VEGFR1, vascular permeability factor receptor, tyrosine-protein kinase FRT) fragment, fused with *Homo sapiens* KDR (kinase insert domain receptor, vascular endothelial growth factor receptor 2, VEGFR2, protein-tyrosine kinase receptor FLK1, CD309) fragment, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;
FLT1, 132-232 precursor fragment (1-101) -KDR, 227-421 precursor fragment (102-296) -glycyl-prolyl-glycyl (297-299) -gamma1 chain H-CH2-CH3 fragment (300-526) [*Homo sapiens* IGHG1*03 hinge 6-15 P13>L (307) (300-309), CH2 (310-419), CH3-CH-S (420-526)]; (305-305':308-308')-bisdisulfide dimer

dalantercept *(105)*

fusion protein for immune applications (FPIA) comprising *Homo sapiens* ACVRL1 (activin A receptor type II-like 1, activin receptor-like kinase 1, ALK1, ALK-1, serine/threonine-protein kinase receptor R3, SKR3, transforming growth factor-beta superfamily receptor type I, TGF-B superfamily receptor type I, TSR-I, HHT2, ORW2) fragment, fused with *Homo sapiens* immunoglobulin G1 Fc fragment;
ACVR2L1, 22-120 precursor fragment (1-99) -threonyl-triglycyl (100-103) -gamma1 chain H-CH2-CH3 fragment (104-328) [*Homo sapiens* IGHG1*03 hinge 8-15 (104-111), CH2 L1.3>A (115), G1>A (118), A115>V (211) (112-221), CH3 S85.3>P (284) (222-328)]; (107-107':110-110')-bisdisulfide dimer

rilonacept *(95)*

[653-glycine][human interleukin-1 receptor accessory protein-(1-339)-peptide (extracellular domain fragment) fusion protein with human type 1 interleukin-1 receptor-(5-316)-peptide (extracellular domain fragment) fusion protein with

human immunoglobulin G1-(229 *C*-terminal residues)-peptide (Fc fragment)], (659-659':662-662')-bisdisulfide dimer

sotatercept *(104)*

fusion protein for immune applications (FPIA) comprising ACVR2A (activin receptor type 2A, activin receptor type IIA) fragment fused with immunoglobulin G1 Fc fragment, and binding activin, a member of the TGF beta family; ACVR2A, 21-135 precursor fragment (1-115) -threonyl-triglycyl linker (116-119) -gamma1 chain H-CH2-CH3 fragment (120-344) [*Homo sapiens* IGHG1*03 hinge (120-127), CH2, A115>V (128-237), CH3 (238-344)]; (123-123':126-126')-bisdisulfide dimer

-cept & -tox

alvircept sudotox [8] *(69)*

N^2-L-methionyl-1-178-antigen CD4 (human clone pT4B protein moiety reduced)(178→248')-protein with 248- L-histidine-249- L-methionine-250- L-alanine-251- L-glutamic acid-248-613-exotoxin A(Pseudomonas aeruginosa reduced)

interferon

albinterferon alfa-2b *(97)*

human serum albumin (585 residues) fusion protein with human interferon α-2b (165 residues)

-kin & -tox

cintredekin besudotox *(92)*

[8] The names and the descriptions of toxins are published in Annex 4-1 of "International Nonproprietary Names (INN) for pharmaceutical substances. Names for radicals, groups & others: comprehensive list (WHO/EMP/QSM/2010.3)"

toxin hIL13-PE38QQR (plasmid phuIL13-Tx)

denileukin diftitox *(78)*

N-L-methionyl-387-L-histidine-388-L-alanine-1-388-toxin (*Corynebacterium diphtheriae* strain C7) (388→2')-protein with 2-133-interleukin 2 (human clone pTlL2-21a)

-mab & -kin

tucotuzumab celmoleukin *(95)*

immunoglobulin G1, anti-(tumor associated calcium signal transducer 1 (KS 1/4 antigen)) (human-mouse monoclonal huKS-IL2 heavy chain) fusion protein with interleukin 2 (human), disulfide with human-mouse monoclonal huKS-IL2 light chain, dimer

-mab & -tox

anatumomab mafenatox *(86)*

immunoglobulin G 1, anti-(human tumor-associated glycoprotein 72) (human-mouse clone pMB125 Fab fragment γ1-chain) fusion protein with enterotoxin A (227-alanine) (*Staphylococcus aureus*) complex with mouse clone pMB125 κ-chain)

citatuzumab bogatox *(99)*

immunoglobulin Fab fusion protein, anti-[*Homo sapiens* tumor-associated calcium signal transducer 1 (TACSTD1, gastrointestinal tumor-associated protein 2, GA733-2, epithelial glycoprotein 2, EGP-2, epithelial cell adhesion molecule Ep-CAM, KSA, KS1/4 antigen, M4S, tumor antigen 17-1A, CD326)], humanized Fab fused with *Bougainvillea spectabilis Willd* rRNA N-glycosidase [type I ribosome inactivating protein (RIP), bouganin], VB6-845; gamma1 heavy chain fragment (1-225) [hexahistidyl (1-6) -humanized VH from 4D5MOC-B (*Homo sapiens* FR/*Mus musculus* CDR, *Homo sapiens* IGHJ4*01, V124>L) [8.8.9] (7-122) -*Homo sapiens* IGHG1*01 CH1-hinge fragment EPKSC (123-225)], (225-219')-disulfide with kappa fusion chain (1'-481') [humanized V-KAPPA from

clone 4D5MOC-B (*Homo sapiens* FR/*Mus musculus* CDR, *Homo sapiens* IGKJ1*01, I126>L) [11.3.9] (1'-112') -*Homo sapiens* IGKC*01 (113'-219') -12-mer furin linker (proteolytic cleavage spacer from Pseudomonas exotoxin A) (220'-231') -*Bougainvillea spectabilis Willd* bouganin fragment (27-276 from precursor, V354'>A, D358'>A, Y364'>N, I383'>A) (232'-481')]

dorlimomab aritox *(66)*

ricin A chain-antibody ST 1 F(ab')2 fragment immunotoxin

moxetumomab pasudotox *(102)*

immunoglobulin Fv fragment fused to *Pseudomonas* toxin, anti-[*Homo sapiens* CD22 (sialic acid-binding Ig-like lectin 2, Siglec-2, SIGLEC2, Leu-14, B-lymphocyte cell adhesion molecule, BL-CAM)], *Mus musculus* monoclonal antibody disulfide stabilized Fv fragment with the variable heavy VH domain fused with the truncated form PE38 of *Pseudomonas aeruginosa* exotoxin A (VH-PE38), disulfide linked with the variable kappa domain (V-KAPPA)];
VH-PE38 (1-476) comprising the VH domain (1-123) [methionyl -*Mus musculus* VH [(IGHV5-12-1*01 -(IGHD)-IGHJ3*01) [8.8.16] (2-123)] fused with a 7-mer linker (124-130) and with the *Pseudomonas aeruginosa* exotoxin A (ETA) PE38 fragment (131-476) [277-638 precursor fragment with del 389-405>N (131-476), containing domain II (131-243) with furin proteolytic cleavage site (152-164), domain Ib (244-267), domain III (268-476)], (45-101')-disulfide with V-KAPPA (1'-108') [methionyl -*Mus musculus* V-KAPPA [(IGHKV10-96*01 -IGKJ1*01) [6.3.9] (2'-108')]

nacolomab tafenatox *(80)*

immunoglobulin G1, anti-(human colorectal tumor antigen C242) Fab fragment (mouse monoclonal r-C242Fab-SEA clone pkP941 γ1-chain) fusion protein with enterotoxin A (*Staphylococcus aureus*), disulfide with mouse monoclonal r-C242Fab-SEA clone pkP941 κ-chain

naptumomab estafenatox *(96)*

immunoglobulin fragment, anti-[trophoblast glycoprotein (TPBG, 5T4)] monoclonal 5T4 gamma1 heavy chain fragment fusion protein [*Mus musculus* VH (5T4V14: H41>P, S44>G, I69>T, V113>G)-IGHG1_CH1)] - [Glycyl-Glycyl-Prolyl] - superantigen SEA/E-120 (synthetic), non-disulfide linked with monoclonal 5T4 kappa light chain [*Mus musculus* V-KAPPA (5T4V18: F10>S, T45>K, I63>S, F73>L, T77>S, L78>V, L83>A)-IGKC]

oportuzumab monatox *(100)*

immunoglobulin scFv fusion protein, anti-[*Homo sapiens* tumor-associated calcium signal transducer 1 (TACSTD1, gastrointestinal tumor-associated protein 2, GA733-2, epithelial glycoprotein 2, EGP- 2, epithelial cell adhesion molecule Ep-CAM, KSA, KS1/4 antigen, M4S1, tumor antigen 17-1A, CD326)] humanized monoclonal antibody scFv fused with *Pseudomonas aeruginosa* exotoxin A; hexahistidyl -humanized scFv [V-KAPPA (*Homo sapiens* IGKV1- 39*01 (78%)-IGKJ1*01, I126>L) [11.3.9] (7-118) -26-mer linker -VH (*Homo sapiens* IGHV7-4-1*02 -(IGHD)-IGHJ4*01, V124>L) [8.8.9] (145-260)] -20-mer linker -*Pseudomonas aeruginosa* exotoxin A (ETA) [277-633 precursor fragment, containing domain II (281-393) with furin proteolytic cleavage site (302-313), domain Ib (394-433), domain III (434-637)] (281-637) -hexahistidyl-lysyl-aspartyl-glutamylleucyl

taplitumomab paptox *(84)*

immunoglobulin G1, anti-(human antigen CD19) (mouse monoclonal B43 γ1-chain), disulfide with mouse monoclonal B43 κ-chain, dimer, disulfide with protein PAP (pokeweed antiviral)

telimomab aritox *(66)*

ricin A chain-antibody T 101 Fab fragment immunotoxin

zolimomab aritox *(80)*

immunoglobulin G1, anti-(human CD5 (antigen) heavy chain) (mouse monoclonal H65-RTA γ1-chain), disulfide with mouse monoclonal H65-RTA light chain, dimer, disulfide with ricin (castor bean A-chain)

-stim (colony stimulating factors)

romiplostim *(97)*

L-methionyl[human immunogloblin heavy constant gamma 1-(227 *C*-terminal residues)-peptide (Fc fragment)] fusion protein with 41 amino acids peptide, (7-7':10,10')-bisdisulfide dimer

-tide

albiglutide *(97)*

([8-glycine]human glucagon-like peptide 1-(7-36)-peptidyl)([8-glycine]human glucagon-like peptide 1-(7-36)-peptidyl)(human serum albumin (585 residues))

cenderitide (105)

natriuretic peptide receptor type B (NPR-B) agonist;
human C-type natriuretic peptide-(32-53)-peptide (CNP-22) fusion protein with eastern green mamba (*Dendroaspis angusticeps*) natriuretic peptide-(24-38)-peptide

dulaglutide *(103)*

glucagon-like peptide-1-immunoglobulin G4 fusion protein, [2-glycyl,16-L-glutamyl,30-glycyl][human glucagon-like peptide 1-(7-37)-peptide] {(8-A>G,22-G>E,36-R>G)-GLP-1(7-37)} fusion protein with tris(tetraglycyl-L-seryl)-L-alanine (linker) fusion protein with des-276-lysine-[57-L-proline,63-L-alanine,64-L-alanine]human immunoglobulin G4 Fc region {(10-S>P)-H-(4-F>A,5-L>A)-CH2-(107-K>-)-CH3 of IGHG4*01}, dimer (55-55':58-58')-bisdisulfide

elsiglutide *(104)*

[2-glycine(A>G),3-glutamic acid(D>E),8-serine(D>S),10-leucine(M>L),11-serine(N>S),16-alanine(N>A),24-alanine(N>A),28-alanine(Q>A)]human glucagon-like peptide 2 (GLP-2) fusion protein with hexalysinamide

vanutide cridificar *(100)*

inactivated diphtheria toxin (carrier) covalently linked to human beta-amyloid protein 42 short fragments: pentadecakis[$N^{6\text{-Lys}}$-(sulfanylacetyl)]-[52-glutamic acid(G>E)]diphtheria toxin *Corynebacterium diphtheriae* thioether with human beta-amyloid protein 42-(1-7)-peptidylcysteine

Others

torapsel *(91)*

42-89-glycoprotein (human clone PMT21:PL85 P-selectin glycoprotein ligand fusion protein with immunoglobulin (human constant region)

transferrin aldifitox *(95)*

a conjugate of the precursor of human serotransferrin (siderophillin) with a primary amine group used to form an amidine with (4-iminobutane-1,4-diyl)sulfanediyl[(3RS)-2,5-dioxopyrrolidine-1,3-diyl]-1,3-phenylenecarbonyl and forming an *N*-benzoyl derivative of a primary amine group of diphtheria [550-L-phenylalanine]toxin from *Corynebacterium diphtheriae*-(26-560)-peptide

verpasep caltespen *(95)*

60 kDa chaperonin 2 (heat shock protein 65 from *Mycobacterium bovis* strain BCG) fusion protein with L-histidylprotein E7 from human papillomavirus type 16.

ANNEX 2

Transliteration of Greek letters in English, French and Spanish

Upper case	Lower case	English	French	Spanish	
A	α	alfa (and **not** alpha)	alfa (and **not** alpha)	alfa	
B	β	beta	bêta	beta	
Γ	γ	gamma	gamma	gamma	
Δ	δ	delta	delta	delta	
E	ε	epsilon	epsilon	épsilon	
Z	ζ	zeta	zêta	**ds**eta	*
H	η	eta	êta	eta	
Θ	θ	theta	thêta	**z**eta	*
I	ι	iota	iota	iota	
K	κ	kappa	kappa	kappa	
Λ	λ	lambda	lambda	lambda	
M	μ	mu	mu	mi	
N	ν	nu	nu	ni	
Ξ	ξ	xi	xi	xi	
O	ο	omicron	omicron	ómicron	
Π	π	pi	pi	pi	
P	ρ	rho	rhô	ro	
Σ	σ	sigma	sigma	sigma	
T	τ	tau	tau	tau	
Y	υ	upsilon	upsilon	ípsilon	
Φ	φ	phi	phi	fi	
X	χ	chi	khi	ji	
Ψ	ψ	psi	psi	psi	
Ω	ω	omega	oméga	omega	

* letters to be avoided

ANNEX 3

The previous naming scheme for monoclonal antibodies

General policies for monoclonal antibodies

- The common stem for monoclonal antibodies is *-mab*.
- Sub-stems for source of product:

a	rat
axo (pre-sub-stem)	rat-murine hybrid
e	hamster
i	primate
o	mouse
u	human
xi	chimeric
zu	humanized

The distinction between chimeric and humanized antibodies is as follows:

A chimeric antibody is one that contains contiguous foreign-derived amino acids comprising the entire variable region of both heavy and light chains linked to heavy and light constant regions of human origin.

A humanized antibody has segments of foreign-derived amino acids interspersed among variable region segments of human-derived amino acid residues and the humanized heavy-variable and light-variable regions are linked to heavy and light constant regions of human origin.

- Sub-stems for disease or target class:

-ba(c)-	bacterial
-ci(r)-	cardiovascular
-fung-	fungal
-ki(n)- (pre-sub-stem)	interleukin
-le(s)-	inflammatory lesions
-li(m)-	immunomodulator
-os-	bone
-vi(r)-	viral

tumours:

-co(l)-	colon
-go(t)-	testis
-go(v)-	ovary
-ma(r)-	mammary
-me(l)-	melanoma
-pr(o)-	prostate
-tu(m)-	miscellaneous

Whenever there is a problem in pronunciation, the final letter of the sub-stems for diseases or targets may be deleted, e.g. *-vi(r)-, -ba(c)-, -li(m)-, -co(l)-*, etc.

Prefix

Should be random e.g. the only requirement is to contribute to a euphonious and distinctive name.

Second word

If the product is radiolabelled or conjugated to another chemical, such as toxin, identification of this conjugate is accomplished by use of a separate, second word or acceptable chemical designation.

If the monoclonal antibody is used as a carrier for a radioisotope, the latter will be listed first in the INN, e.g. *technetium (^{99m}Tc) pintumomab (86)*.

***-toxa-* infix**

For monoclonals conjugated to a toxin, the infix *-toxa-* can be inserted either into the first (main) name or included in the second word.