

**International Nonproprietary Names (INN)  
for biological and biotechnological substances**  
(a review)



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# **International Nonproprietary Names (INN) for biological and biotechnological substances**

**(a review)**



**Programme on International Nonproprietary Names (INN)**  
**Quality Assurance and Safety: Medicines**  
**Medicines Policy and Standards**

**International Nonproprietary Names (INN)  
for biological and biotechnological substances**  
**(a review)**

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# 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 *-actide* 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 / biotechnology 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.

With 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 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 <sup>(1)</sup>**

## **Alimentary tract and metabolism**

insulins (see item 4.17).

## **Anti-infectives**

antimicrobial, bactericidal permeability increasing polypeptides  
(see item 4.1)

human papilloma virus (see item 4.16).

## **Antineoplastics**

peptide vaccines / recombinant vaccines (see item 4.24)  
toxins (see item 4.30).

## **Blood and agents acting on the haemopoietic system**

antithrombins (see item 4.3)  
blood coagulation cascade inhibitors (see item 4.4)  
blood coagulation factors (see item 4.5)  
erythropoietin type blood factors (see item 4.8)  
heparin derivatives including low molecular mass heparins (see item 4.13)  
hirudin derivatives (see item 4.14)  
thrombomodulins (see item 4.29).

## **Immunomodulators and immunostimulants**

colony stimulating factors (see item 4.6)  
interferons (see item 4.18)  
interleukin receptor antagonists (see item 4.19)  
interleukin type substances (see item 4.20)  
monoclonal antibodies (see item 4.21)  
receptor molecules, native or modified (see item 4.27)  
tumor necrosis factor antagonists (see item 4.31).

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

growth hormone (GH) derivatives (see item 4.11)  
growth hormone antagonists (see item 4.12)  
oxytocin derivatives (see item 4.22)  
pituitary / placental glycoprotein hormones (see item 4.25)  
pituitary hormone-release stimulating peptides (see item 4.26)  
synthetic polypeptides with a corticotropin-like action (see item 4.28)  
vasoconstrictors, vasopressin derivatives (see item 4.32).

## **Various**

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 4.28), -pressin (see item 4.32), -relin (see item 4.26),  
-tocin (see item 4.22)) (see item 4.23).

## 2. CURRENT STATUS OF EXISTING STEMS OR SYSTEMS FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES<sup>(1) (2) (3) (4) (5) (6) (7) (8)</sup>

### 2.1 Groups with respective stems

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

## 2.2 Groups with respective pre-stems

Name of the group	Pre-stem
antimicrobial, bactericidal permeability increasing polypeptides	- <i>ganan</i>

## 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
human papilloma virus
peptide vaccines / recombinant vaccines
thrombomodulins
toxins

### **3. GENERAL POLICIES FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES**

#### **3.1 General policies for blood products <sup>(5)</sup>**

- 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 <sup>(5)</sup>**

- INNs have been assigned to some fusion proteins. If there exists a stem for one or the other part of the fusion protein, this stem should be brought into the name. This would allow 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 <sup>(2)</sup>**

In 2005, the Nomenclature Scheme for Gene Therapy Products was formally adopted. The scheme is attached here below.

## Two-Word Scheme

	prefix	infix	suffix
<b>word 1</b> (gene component)	to contribute to the distinctive name  e.g. <i>al-</i> ; <i>bet-</i> ; <i>val-</i>	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. <i>-ermin-</i> : growth factor <i>-kin-</i> : interleukin <i>-lim-</i> : immunomodulator <i>-mul-</i> : multiple gene <i>-tusu-</i> : tumour suppression	<i>-(a vowel)gene</i>  e.g. <i>-(o)gene</i>
<b>word 2</b> (vector component)	to contribute to the distinctive name	e.g. <i>-adeno-</i> : adenovirus <i>-cana-</i> : canarypox virus <i>-herpa-</i> : herpes virus <i>-lenti-</i> : lentivirus <i>-morbilli-</i> : paramyxoviridae morbillivirus <i>-parvo-</i> : adeno-associated virus (parvoviridae dependovirus) <i>-retro-</i> : other retrovirus <i>-vari-</i> : vaccinia virus	<i>-vec</i> (non-replicating viral vector) <i>-repvec</i> (replicating viral vector)
			<i>-plasmid</i> (plasmid vector)

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

### 3.4 General policies for glycosylated compounds <sup>(9)</sup>

#### For glycoproteins / glycopeptides

- Identification of the group with a stem, e.g. for erythropoietin: *-poetin*, indication of differences in the amino acid chain by using a random prefix and indication of differences in the glycosylation pattern by another designator, expressed by a Greek letter spelt in full and added as second word to the name (e.g. *epoetin alfa* (66)). The Greek letters are used in the Greek alphabetical order.
- Identification of the group with a word, e.g. interferon. Subgroups are identified by a Greek letter spelt in full and added as second word to the name; differences in the composition of the amino acid sequence are indicated by using an Arabic figure; different compounds,

including different glycosylation pattern, are indicated by a small letter (e.g. *interferon beta* (73), *peginterferon alfa-2a* (84)).

### 3.5 General policies for immunoglobulins <sup>(10) (11)</sup>

Not to select an INN for each of immunoglobulins.

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 <sup>(1) (3)</sup>

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

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

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

tumours:

<i>-co(l)-</i>	colon
<i>-go(t)-</i>	testis
<i>-go(v)-</i>	ovary
<i>-ma(r)-</i>	mammary
<i>-me(l)-</i>	melanoma
<i>-pr(o)-</i>	prostate
<i>-tu(m)-</i>	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 (<sup>99m</sup>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.

### 3.7 General policies for non-glycosylated compounds <sup>(9)</sup>

#### 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 <sup>(5)</sup>

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 INN system.

### 3.9 General policies for transgenic products <sup>(5)</sup>

- 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 <sup>(5) (6) (7) (8)</sup>

- 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 pharmacopoeial monograph.
- During the 1993 INN Consultation, it was agreed that the prerequisite for an INN application for a recombinant vaccine would be fulfilled if the manufacturer was able to provide all information outlined in the guidelines Definition of INNs for Substances Prepared by Biotechnology (WHO / Pharm S / Nom 1348<sup>(12)</sup>).
- During the 1998 Consultation, with regard to 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<sup>1</sup> (epitopes involved in immune response formation): since these peptides are chemically well defined, their naming will be less problematic.

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<sup>1</sup> The definition of peptide vaccines can be found in item 4.24

## 4. SUMMARY OF INN ASSIGNED TO BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES

(1) (3) (4) (8) (9)(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)<sup>2</sup>, *omiganan* (89), *pexiganan* (78).

### 4.2 Antisense oligonucleotides

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

*afovirsen* (97), *alicaforsen* (97), *aprinocarsen* (97), *cenersen* (97), *fomivirsen* (97), *oblimersen* (97), *trabedersen* (97), *trecovirsen* (97).

### 4.3 Antithrombins

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

### 4.4 Blood coagulation cascade inhibitors

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

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

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<sup>2</sup> The numbers in parentheses indicate the Proposed list number

## 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 parenthesis after the name.

blood coagulation VII: *-eptacog*  
*eptacog alfa (activated) (77)*, *vatreptacog alfa (activated) (97)*

blood factor VIII: *-octocog*  
*beroctocog alfa (95)*, *moroctocog alfa (72)*, *octocog alfa (73)*

blood factor IX: *-nonacog*  
*nonacog alfa (77)*.

## 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)* (platelet stimulating factor (through Mpl receptor))

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

enzymes with superoxide dismutase activity: -*dismase*

- *ledismase* (70), *sudismase* (58)
- isomerase: *orgotein* (31), *pegorgotein* (72)

plasminogen activator combined with another enzyme: -*diplase*

*amediplase* (79)

tissue-type-plasminogen activators: *-teplase*

*alteplase* (73), *anistreplase* (59), *desmoteplase* (80), *duteplase* (62),  
*lanoteplase* (76), *monteplase* (72), *nateplase* (73), *pamiteplase* (78),  
*reteplase* (69), *silteplase* (65), *tenecteplase* (79)

urokinase-type-plasminogen activators: *-uplase*

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

others:

*agalsidase alfa* (84), *agalsidase beta* (84), *alfimeprase* (85),  
*alglucerase* (68), *alglucosidase alfa* (91), *dornase alfa* (70), *epafipase* (85),  
*eufausease* (84), *galsulfase* (92), *glucarpidase* (92), *hyalosidase* (50),  
*hyaluronidase* (1), *idursulfase* (90), *imiglucerase* (72), *laronidase* (86),  
*pegademase* (63), *penicillinase* (10), *ranpirnase* (81), *streptodornase* (6),  
*tilactase* (50).

## 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).

INNs with different amino acid sequence 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), *amolimogene bepiplasmid* (selected during the 42<sup>nd</sup> Consultation), *beperminogene perplasmid* (95), *contusugene ladenovec* (97), *sitimogene ceradenovec* (97), *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 tumor 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), *trafermin* (74),  
*velafermin* (94)

leukemia-inhibiting factors: *-filermin*

*emfilermin* (82)

tumour necrosis factors: *-nermin*

*ardenermin* (88), *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)

**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) (growth hormone release-stimulating peptides, see item 4.26), *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), 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), 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 Hormone-release inhibiting peptides

**The common stem for 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 Human papilloma virus

*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.**

#### 4.17 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, or represent modifications of the amino acid sequence, i.e. *insulin aspart* (76).**

*biphasic insulin injection (16), compound insulin zinc suspension (06), dalanated insulin (14), globin zinc insulin injection (06), insulin argine (58), insulin aspart (76), insulin defalan (37), insulin detemir (80), insulin glargine (76),*

*insulin glulisine (84), insulin human (48), insulin lispro (72), insulin zinc suspension (amorphous) (04), insulin zinc suspension (crystalline) (04), isophane insulin (04), neutral insulin injection (15), protamine zinc insulin injection (06).*

## 4.18 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 was barred as these names had already been registered as trade marks. The system adopted was then 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.**

*albinterferon alfa-2b (97), interferon alfa (73), interferon alfacon-1 (77), interferon beta (73), interferon gamma (73), peginterferon alfa-2a (84), peginterferon alfa-2b (84).*

## 4.19 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: *-trakina*

*pitrakina (87).*

## 4.20 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-1 $\alpha$  analogues and derivatives: *-onakin*

*pifonakin* (77)

interleukin-1 $\beta$  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*

*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*

*cintradekin besudotox* (92)

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

*iboctadekin* (92)

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

*abrineurin* (84)

## 4.21 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), *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), *nacolomab tafenatox* (80), *naptumomab estafenatox* (96), *nerelimomab* (81), *odulimomab* (81), *oregovomab* (86), *satumomab* (81), *sulesomab* (86), *taplitumomab paptox* (84), *technetium (<sup>99m</sup>Tc) fanolesomab* (86), *technetium (<sup>99m</sup>Tc) nofetumomab merpentan* (81), *technetium (<sup>99m</sup>Tc) pintumomab* (86), *telimomab aritox* (66), *tositumomab* (80), *vepalimomab* (80), *zolimomab aritox* (80).

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

*adalimumab* (85), *adecatumumab* (90), *atorolimumab* (80), *belimumab* (89), *bertilimumab* (88), *canakinumab* (97), *denosumab* (94), *efungumab* (95),

*exbivirumab* (91), *gantenerumab* (97), *golimumab* (91), *ipilimumab* (94), *iratumumab* (94), *lerdelimumab* (86), *lexatumumab* (95), *libivirumab* (91), *mapatumumab* (93), *metelimumab* (88), *morolimumab* (79), *nebacumab* # (66), *ofatumumab* (93), *panitumumab* (96), *pritumumab* (89), *raxibacumab* (92), *regavirumab* (80), *sevirumab* (66), *stamulumab* (95), *tremelimumab* (97), *tuvirumab* (66), *votumumab* (80), *zalutumumab* (93), *zanolimumab* (92), *ziralimumab* (84).

#### **-ximab (chimeric origin)**

*abciximab* (80), *basiliximab* (81), *bavituximab* (95), *cetuximab* (82), *clenoliximab* (77), *ecromeximab* (87), *galiximab* (89), *infliximab* (77), *keliximab* (81), *lumiliximab* (90), *pagibaximab* (93), *priliximab* (80), *rituximab* (77), *teneliximab* (87), *vapaliximab* (87), *volociximab* (93).

#### **-zumab (humanized origin)**

*alemtuzumab* (83), *apolizumab* (87), *aselizumab* (88), *bapineuzumab* (93), *bevacizumab* (86), *bivatuzumab* (86), *cantuzumab mertansine* (89), *cedelizumab* (81), *certolizumab pegol* (97), *daclizumab* (78), *eculizumab* (87), *efalizumab* (85), *epratuzumab* (82), *erlizumab* (84), *felvizumab* (77), *fontolizumab* (87), *gemtuzumab* (83), *ibalizumab* (97), *inotuzumab ozogamicin* (92), *labetuzumab* (85), *lintuzumab* (86), *matuzumab* (88), *mepolizumab* (81), *motavizumab* (95), *natalizumab* (79), *nimotuzumab* (94), *ocrelizumab* (95), *omalizumab* (84), *palivizumab* (79), *pascolizumab* (87), *pertuzumab* (89), *pexelizumab* (86), *ranibizumab* (90), *reslizumab* (85), *rovelizumab* (81), *ruplizumab* (83), *sibrotuzumab* (86), *siplizumab* (87), *sontuzumab* (94), *tadocizumab* (94), *talizumab* (89), *tefibazumab* (92), *teplizumab* (97), *tocilizumab* (90), *toralizumab* (87), *trastuzumab* (78), *tucotuzumab celmoleukin* (95), *urtoxazumab* (90), *visilizumab* (84), *yttrium <sup>90</sup>Y tacatuzumab tetraxetan* (93).

## **4.22 Oxytocin derivatives**

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

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

## **4.23 Peptides and glycopeptides (for special groups of peptides see -actide (see item 4.28), -pressin (see item 4.32), -relin (see item 4.26), -tocin (see item 4.22))**

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

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

angiogenesis inhibitor: *cilengitide* (81)

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

anti-inflammatory: *icrocaptide* (89)

antiarrhythmic: *rotigaptide* (94)

antidepressant: *nemifitide* (87)

antidiabetic: *albiglutide* (97), *amlintide* (76), *exenatide* (89), *liraglutide* (87),  
*pramlintide* (74), *seglitide* (57)

antidiarrhoeal: *lagatide* (75)

antiobesity drug: *obinepitide* (96)

antithrombotic: *eptifibatide* (78)

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

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

cardiac stimulant: *carperitide* (65)

diagnostic: *betiatide* (58), *bibapcitide* (78), *ceruletide* (34), *depreotide* (80),  
*mertiatide* (60), *pendetide* (70), *technetium* (<sup>99m</sup>Tc) *apcitide* (86),  
*teriparatide* (50)

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

gastro-intestinal functions normalizing agent: *teduglutide* (90), *linaclotide* (97)

growth stimulant-veterinary: *nosiheptide* (35)

gut motility increasing: *ociltide* (52)

hormone analogue: *semparatide* (80)

immunological agents - antineoplastics: *almurtide* (74), *delmitide* (92),  
*disomotide* (94), *edratide* (89),

*goralatide (72), mifamurtide (95),  
murabutide (49), ovemotide (94),  
pentigetide (60), pimelautide (53),  
prezotide copper acetate (67),  
rolipoltide (94), romurtide (61),  
tabilautide (60), temurtide (60),  
tigapotide (95), tiplimotide (82)*

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

kallicrein inhibitor: *ecallantide (93)*

melanocortin receptor agonist: *bremelanotide (95)*

neuromodulator: *ebiratide (56)*

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

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

sedative: *emideltide (70)*

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

wound healing agent: *rusalatide (96)*

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

#### 4.24 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:

*disomotide (94), ovemotide (94).*



## 4.25 Pituitary / placental glycoprotein hormones

The names selected by the IUPAC-IUB have, to date, been chosen for compounds with identical amino acid sequence as the naturally occurring human hormones. Addition of a Greek letter as second part of the name will allow differentiating for 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)

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).

## 4.26 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), *leuporelin* (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), *pralmorelin* (77), *rismorelin* (74), *sermorelin* (56), *somatorelin* (57), *tabimorelin* (86), *tesamorelin* (96)

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)

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

#### 4.27 Receptor molecules, native or modified

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

A preceding infix should designate the target.

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

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)

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

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

other: *atacicept* (95) (**fusion protein**)

see item 4.31 *-nercept*.

#### 4.28 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).*

#### 4.29 Thrombomodulins

*thrombomodulin alfa (94).*

#### 4.30 Toxins

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

#### 4.31 Tumor necrosis factor antagonists

**The common stem for tumor necrosis factor antagonists is *-nercept*.**

*etanercept (81), lenercept (72), onercept (86), pegsunercept (95).*

#### 4.32 Vasoconstrictors, vasopressin derivatives

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

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

#### 4.33 Various

- *angiotensin II (65)*: 5-L-isoleucineangiotensin II (the source of the material should be indicated)
- *angiotensinamide (12)*: N-{1-{N-{N-{N-[N-(N<sup>2</sup>-asparaginyllarginyl)valyl]tyrosyl}valyl}histidyl}prolyl}-3-phenylalanine
- *calcitonin (80)*: a polypeptide hormone that lowers the calcium concentration in blood (the species specificity should be indicated in brackets behind the name)
- *epelestat (92)*: human recombinant neutrophil elastase inhibitor, bovine pancreatic trypsin inhibitor (BPTI) homologue

- *edifoligide* (89): oligonucleotide
- *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<sub>0</sub> (human  $\alpha_2\beta_2$  tetrameric subunit),  $\alpha$ -chain 99,99'-diamide with fumaric acid
- *hemoglobin raffimer* (89)
- *iropact* (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* (<sup>131</sup>I) (33): macroaggregated iodinated (<sup>131</sup>I) human albumin
- *macrosalb* (<sup>99m</sup>Tc)(33): technetium (<sup>99m</sup>Tc) labelled macroaggregated human serum albumin
- *metenkefalin* (97): L-tyrosylglycylglycyl-L-phenylalanyl-L-methionine  $\beta$ -endorphin human-(1-5)-peptide
- *metreleptin* (82): N-methionylleptin (human)
- *mirostipen* (85): [23-methionine] human myeloid progenitor inhibitory factor 1-(23-99)-peptide
- *muromonab-CD3* (59): a biochemically purified IgG<sub>2a</sub> immunoglobulin consisting of a heavy chain of approx. 50,000 daltons and a light chain of approx. 25,000 daltons. It is manufactured by a process involving the fusion of mouse myeloma cells to lymphocytes from immunized animals to produce a hybridoma which secretes antigen-specific antibodies to the T3 antigen of human T-lymphocytes.
- *nagrestipen* (76): 26-L-alaninelymphokine MIP 1 $\alpha$  (human clone pAT464 macrophage inflammatory)
- *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
- *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  $\alpha,\alpha'$ -  
 [[[1*S*)-1-[[5-(phosphonoxy)pentyl]carbonyl]pentane-1,5-  
 diyl]bis(iminocarbonyl)]bis[ $\omega$ -methoxypoly(oxyethane-1,2-diyl)]
- *secretin (01)*: hormone of the duodenal mucosa which activates the pancreatic secretion and lowers the blood-sugar level
  - *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  $\alpha$ )
  - *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)
  - *votucalis (96)*: methionyl[145-leucine]FS-HBP2 (*Rhipicephalus appendiculatus* (Brown ear tick) Female-Specific Histamine-Binding Protein 2).

## 5. CURRENT CHALLENGES

- The INN Expert Group, when selecting names for recombinant proteins, has to deal not with substances of well-defined structure 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 its 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 these products.
- Clearly, the INN nomenclature of biological medicinal products is an area of increasing complexity.

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21. Generic names for genetically-engineered insulins, *WHO/Pharm S/Nom 737* (1980-1983)

\* *Theses documents are available on the INN Programme Website at:*

<http://www.who.int/medicines/services/inn/en/>