EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 January 2018
EMA/CHMP/BWP/133540/2017
Committee for Medicinal Products for Human Use (CHMP)

Guideline on quality aspects included in the product information for vaccines for human use

Draft agreed by BWP, VWP, CMDh, QRD, SmPC AG	October 2017
Adopted by CHMP for release for consultation	25 January 2018
Start of public consultation	1 February 2018
End of consultation (deadline for comments)	31 July 2018
Agreed by BWP, VWP, CMDh, QRD, SmPC AG	
Adopted by CHMP	
Date for coming into effect	

This guideline replaces 'Guideline on pharmaceutical aspects of the product information for human vaccines' (EMEA/CPMP/BWP/2758/02).

Comments should be provided using this template. The completed comments form should be sent to Kaidi.koiv@ema.europa.eu

Keywords	Vaccine, product information, common name, SmPC, label, Package Leaflet, active substance, residuals, adjuvants, excipients, storage.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Executive summary

This guideline describes the information on the quality aspects to be included in the Product Information (PI) of vaccines for human use.

1. Introduction (background)

The purpose of this document is to provide applicants and regulators with harmonised guidance on the quality aspects to be considered in the Summary of Product Characteristics (SmPC), Package Leaflet (PL) and labelling for vaccines for human use. This guideline should be read in conjunction with other guidelines/documents which are referenced in this document. Applicants are advised to take this guideline into account when submitting applications for Marketing Authorisation (MA) for new vaccines, and may consider it on the occasion of applying for renewals or updates of the product information of already approved vaccines for human use.

2. Scope

The guideline provides guidance on the content and presentation of the pharmaceutical particulars and quality aspects applicable to the product information (SmPC, labelling, and PL) for vaccines for human use intended for the prevention of infectious diseases, whether administered before infection occurs or for post-exposure prophylaxis. The need for special guidance arises from the complexity of many aspects of vaccine composition and formulation and use.

Guidance specific to the description of strains for influenza vaccines appears in the "Guideline on influenza vaccines – submission and procedural requirements"[1], published by the Agency. All other aspects of this guideline apply to influenza vaccines.

3. Legal basis

This guideline has to be read in conjunction with the introduction and general principles (4) and part I of the Annex I to Directive 2001/82 or 2001/83 as amended, as well as the Guideline on Summary of Product Characteristics[2], Guideline on the acceptability of names for human medicinal products processed through the centralised procedure, Guideline on Excipients in the label and package leaflet of medicinal products for human use, Note for guidance on stability testing of new drug substances and products, Note for guidance on stability testing of existing drug substances and products, Note for guidance on maximum shelf life of sterile products after first opening or following reconstitution and Guideline on declaration of storage conditions: A: in the product information of medicinal products B: for active substances.

[1] Guideline on influenza vaccines – submission and procedural requirements http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/03/WC500223481.pdf

[2] Guideline on Summary of Product Characteristics http://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/c/smpc_guideline_rev2_en.pdf

SUMMARY OF PRODUCT CHARACTERISTICS

The quality sections of the SmPC are 1, 2, 3, 6.1, 6.2, 6.3, 6.4, 6.5 and 6.6.

For some aspects, sections 4.3, 4.4 and 4.8 are also referred to.

In general promotional statements e.g. serum-free cells, preservative-free, latex-free are not allowed to be included.

1. NAME OF THE MEDICINAL PRODUCT

The entries under Section 1 in the SmPC for vaccines should appear in the following order:

- Invented name,
- [strength],
- pharmaceutical form,
- common name of the vaccine,

and take into account the following guidance:

Invented name of the medicinal product

European Rules for invented names for medicinal products should be observed. For vaccines composed of several serotypes the invented name may include the number of serotypes present[3].

Strength

The strength should be included if different concentrations of a vaccine are approved for different age and risk groups in one MA. In all other cases it is acceptable not to include the strength.

Pharmaceutical form

The pharmaceutical form should be stated for all vaccines. The appropriate single full Standard Term[4] of the European Pharmacopoeia, or a combined Standard Term, should be used to express the pharmaceutical form. This is particularly important in case of a particular safety reason or risk of misadministration of the vaccine (e.g. nasal spray suspension, oral suspension).

The container should not be included in the pharmaceutical form unless it is part of the Standard Term.

As a result, in the case of a pre-filled syringe presentation of a vaccine, the pharmaceutical form of the pre-filled syringe presentation should always be expressed as "<solution> <suspension> for injection in pre-filled syringe".

Common name of the vaccine

The common name should be understood to mean the title of the relevant European Pharmacopoeia monograph, where one exists. In cases where there is no European Pharmacopoeia monograph, the stylistics and precedents of European Pharmacopoeia monograph titles should be observed[5]. Generally the common name is defined by the infectious agents it is intended to protect from, e.g. meningococcocal group B vaccine, Ebola vaccine, dengue vaccine, or the disease it is intended to prevent, e.g., Herpes zoster vaccine. The following terms should be included in parenthesis, if applicable:

[3] Guideline on the acceptability of names for human medicinal products processed through the centralised procedure http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2014/06/WC500167844.pdf
[4] List of standard terms for pharmaceutical dosage forms, routes of administration, and containers https://www.edqm.eu/en/standard-terms-590.html
[5] Technical Guide for the elaboration of monographs on vaccines and other immunological human medicinal products https://www.edqm.eu/en/technical-guides-589.html

- Adsorbed: the vaccine antigen is adsorbed to aluminium salts.
- Adjuvanted: the vaccine contains an adjuvant or a mixture of adjuvants.
- Inactivated: the vaccine contains killed organisms.
- rDNA: the vaccine antigen is manufactured using recombinant DNA technology. However the word 'rDNA' should not be added to the common name if only a carrier protein is made by recombinant DNA technology.
- Live: the vaccine consists of replicating infectious organisms. The word "attenuated" should not be included in the common name.

For vector-based and chimeric vaccines the term "rDNA" should be used. If the strain is replication competent "live" should also be added. As regards multivalent vaccines, no wording on the serotypes should be included in the common name.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The principal entries under Section 2 in the SmPC should appear in the following order:

- Qualitative and quantitative declaration of each active substance,
- Qualitative and quantitative declaration of any adjuvant or adsorbant present,
- Origin of the active substance, if applicable
- Residues of clinical relevance, if applicable
- Excipients with known effects, if applicable
- a reference to the full list of excipients in 6.1,

and take into account the following guidance:

Active substance(s)

The content of the active substance(s), should be expressed per dose unit (e.g. "One dose (0.5 ml) contains:"). The amount (range) of the carrier protein should be given here as well. Examples are provided in the Annex.

For multivalent vaccines containing various serotypes of a pathogen, all serotypes need to be specified. For combination vaccines such as DTaP vaccines, the active substances would ideally appear in the order of the relevant monograph title of the European Pharmacopoeia, where one exists.

Abbreviations for active substance names (including carrier protein) should not be used in the product information. However the abbreviation CRM197 (a non-toxic mutant of diphtheria toxin) is considered to be acceptable.

Directive 2001/83/EC requires that in section 2 of SmPCs, the usual common name of active substances shall be used. As there are no INNs for vaccine antigens, each active substance name should be in conformity with European Pharmacopoeia monograph terminology for vaccine antigens in so far as is possible. For non-pharmacopoeial active substances, the active substance name should ideally be expressed according to its formal Latin/Greek name, or according to the disease being protected against, taking historical and pharmacopoeial precedents for the naming of similar vaccine antigens into account.

Taxonomic names for cellular microorganisms should be italicised. Names of microbial genera should not be abbreviated. Generally, for bacteria and viruses, the strain, serotype or other appropriate sub-species designation should be included in the name of each antigen, if relevant.

The origin of the active substance should be defined briefly. Thus the nature of any cellular system(s) used for production and if relevant, the use of recombinant DNA technology should be described, following the pattern set by the following examples:

- "produced in human diploid (MRC-5) cells";
- "produced in *Escherichia coli* cells by recombinant DNA technology";

- “produced in chick-embryo cells”.

For combination vaccines, the information on the cellular system(s) used for production may be presented as (a) footnote(s) within section 2.

Otherwise, the inclusion of a mention of the production process in vaccine active substance names should normally be restricted to the use of the following terms:

- "Live, attenuated" (in the case of vaccines containing living micro-organisms),
- "Inactivated" (in the case of vaccines containing killed micro-organisms).

In case the vaccine consists of genetically modified organisms the following sentence should be added:

– “This product contains genetically modified organisms (GMOs)”.

Adjuvants/adsorbants

If an adjuvant or adsorbant is present in the vaccine, it should be included in Section 2. Qualitative and Quantitative Composition. European Pharmacopoeia nomenclature should be employed where possible, with the exception that “aluminium hydroxide, hydrated, for adsorption” should be written as “aluminium hydroxide, hydrated” and “aluminium phosphate for adsorption” should be given as “aluminium phosphate”.

Aluminium compounds are normally referred to as adsorbants. The quantitative declaration of aluminium compounds should be in terms of the quantity of Al^{3+} per dose.

For multivalent and combination vaccines in particular, and also for monovalent vaccines where this is found convenient, the qualitative and quantitative particulars for the adjuvant(s)/adsorbant(s) may be presented as (a) footnote(s) within section 2 of the SmPC. Footnotes should be linked to the active substance(s) concerned (see Attachment 2).

Residues of clinical relevance

For residues of clinical relevance a statement should be included e.g. the vaccine may contain traces of neomycin. Reference to section 4.3 and/or sections 4.4 and/or 4.8 should be made as applicable.

Excipients

Excipients known to have a recognised action or effect should be listed qualitatively and quantitatively under the heading ‘Excipient(s) with known effect’. The content should be given in micrograms or milligrams using the spelled out terms instead of µg or mg respectively.

Reference to sections 4.3, 4.4 and/or 4.8 should be made as applicable.

For all other excipients, a reference should be included ‘For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

The pharmaceutical form should be described by the same Standard Term as used in section 1. In case the container has a tradename this needs to be included in section 3.

A visual description of the appearance of the different vaccine items, if applicable should be given here. In case of vaccines to be reconstituted or mixed before use, the appearance before reconstitution or mixing should be stated in section 3. Appearance of the vaccine after reconstitution or mixing should be stated in sections 4.2 and 6.6.

4. CLINICAL PARTICULARS

Certain residuals such as residues of antibiotic, other antimicrobial agents, host cell proteins and some chemicals used in production of vaccines are known allergens with a potential for inducing undesirable effects.

For residues of clinical relevance and excipients with known effect, contraindications and/or warning statements as well as adverse events specific to excipients or residues should be included in the relevant sections 4.3, 4.4 and/or 4.8 as appropriate[6].

In section 4.4 the following statement on traceability should be included:

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

The excipients should be listed in accordance with the SmPC Guideline[2] using the appropriate common names. As with all excipients, preservatives should be listed qualitatively but not quantitatively in section 6.1.

Residues of reagents used in production should not be listed in section 6.1. Certain residues such as residues of antibiotic or other antimicrobial agents used in production that are known allergens with a potential for inducing undesirable effects should, however, be mentioned in section 2 with reference to section 4.3,4.4 or 4.8 as applicable.

For vaccines, which are presented in more than one container or in dual-chamber syringes, the excipients should be listed per container or per chamber.

For established media with widely–known composition used as complex-multicomponent diluents in the formulation of vaccine drug products, suitable short descriptions may be acceptable in place of very long lists of all the substances present in the media, if justified. In this case, it is recommended to summarise the composition of the media in broad terms (e.g. Medium 199 containing vitamins, mineral salts and amino acids). Media components with known effect (e.g. phenylalanine) should still, however, be mentioned in the appropriate sections.

Abbreviations for excipients should not be used in the SmPC or PL. However, where justified by space constraints, abbreviations for excipient names may appear on the labelling, on condition that these abbreviations are designated in SmPC section 6.1 and in the respective section of the PL.

Adjuvants and adsorbants should not be listed in section 6.1. However, if such materials are present in the vaccine, a reference to section 2 should be made.

6.2 Incompatibilities

Only pharmaceutical (i.e. physical, chemical or biological) incompatibilities should be stated in section 6.2.

The appropriate standard QRD[7] statement i.e. <Not applicable>, <In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products>, or <This vaccine must not be mixed with other medicinal products except those mentioned in section 6.6> should appear.

6.3 Shelf life

The shelf-life declaration(s) should be in accordance with the SmPC Guideline and with related guidance documents[8,9,10]addressing the shelf lives of un-reconstituted and reconstituted vaccines as necessary.

[6] Guideline on Excipients in the label and package leaflet of medicinal products for human use https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/c/guidelines_excipients_july_2013_rev_1.pdf (currently under revision); refer also http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001683.jsp&mid=WC0b01ac05808c01f6

[7] QRD product information templates for Summary of Product characteristics (SmPC), labelling and Package leaflet (PL) Compilation of QRD decisions on stylistic matters in product information and Compilation of QRD decisions on the use of terms are updated and published here: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000134.jsp

[8] Note for guidance on stability testing of new drug substances and products, http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002651.pdf

The expression of the shelf-life should be in accordance with the current QRD template.

6.4 Special precautions for storage

The statement on storage and/or transport conditions included in section 6.4 of the SmPC is intended to inform the end user only. Compliance to Good Distribution Practice should be respected in all circumstances.

The declaration of the precautions for storage should be in accordance with the SmPC Guideline[2] and with related guidance documents[,,11]

In case appropriate stability data are available which confirm the quality of the vaccine, when stored at non-standard temperatures, this information might be added in section 6.4. However the storage at non-standard temperatures should be limited to a maximum period of 72 hours. The statement on storage at non-standard temperatures should be expressed as given in the example below:

"Stability data indicate that the vaccine components are stable for x hours when stored at temperatures from y°C to z°C. At the end of this period <Invented Name> should be used immediately or discarded".

6.5 Nature and contents of container

The declaration of the nature and contents of the container(s) should be in accordance with the SmPC Guideline and with related guidance documents (see list of references).

In the case of multidose presentations, the number of doses per container should be stated.

6.6 Instructions for disposal <and other handling>

In the case of vaccines intended for reconstitution, the appearance of the vaccine before reconstitution is described in section 3, while the appearance of the vaccine following reconstitution needs to be given here.

For all vaccines, there should be instructions to check the appearance of the vaccine before administration. Additional instructions on the handling should be added as necessary.

Information necessary for the pharmacist or other healthcare professional to prepare the vaccine before administration should appear in section 6.6.

For the safe disposal of the vaccine, any material which has come into contact with the vaccine, and/or waste material, appropriate instructions should be given in accordance with local requirements.

[9] Note for guidance on stability testing of existing drug substances and products
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003466.pdf
[10] Note for guidance on maximum shelf life of sterile products after first opening or following reconstitution
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003476.pdf
[11] Guideline on declaration of storage conditions: A: in the product information of medicinal products B: for active substances
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003468.pdf

LABELLING

European guidance documents and templates provide comprehensive guidance on labelling (see references). For vaccines, the following additional guidance should be taken into account.

Outer Packaging

For the statement of active substances, the active substance(s), and the adjuvant/adsorbant, if present, should be expressed qualitatively, and quantitatively per dose unit, as they appear in section 2 of the SmPC, with the exception that, in the case of space constraints, abbreviations for certain adjuvants or adsorbants, as designated in the SmPC, may be acceptable in special circumstances.

For multidose presentations, the number of doses in the container(s) should be stated. Information about the cellular systems used as production substrates may be omitted from the carton labelling.

The list of excipients should appear on the carton labelling and be expressed as in section 6.1 of the SmPC. However, where there are space constraints, abbreviations for certain excipients, as designated in the SmPC, may be acceptable.

For cartons containing ancillary items such as swabs, needles the labelling should include a list of all components. In case the container has a tradename it needs to be stated on the outer packaging.

A full statement of the precautions for disposal of unused product and/or waste material should appear on the outer packaging, unless space constraints prevent this, in which case a reference to the appearance of the disposal directions in the PL is sufficient.

Small immediate packaging

The common name may be abbreviated in case of severe space constraints (e.g. MMRV vaccine). Pharmaceutical form short terms according to the current "List of Standard Terms of the European Pharmacopoeia" will be considered on a case-by-case basis in case of space constraints. If used, the pharmaceutical form, patient-friendly term should be added in brackets in section 3 of the SmPC. In cases of severe space constraints, the pharmaceutical form may be omitted.

Peel-off labels

MA Holders may consider the addition of peel-off labels to the immediate packaging in the context of improving traceability, which could be used for inserting immunisation details into patient records.

PACKAGE LEAFLET (PL)

European guidance documents and templates provide comprehensive guidance on PLs. As required by Directive 2001/83/EC, the package leaflet should be drawn up in accordance with the SmPC, and be written in clear and understandable terms for the user. As in the SmPC, the full Standard Terms should be used in section 6, as there are no space limitations in the PL.

The nature of any cellular system used for production, and if relevant the use of recombinant DNA technology, should be mentioned in section 6 of the PL in a manner consistent with the SmPC, including the use of the expression "produced in XXX cells <by recombinant DNA technology>" and including the statement "This product contains genetically modified organisms (GMOs)", where appropriate.

In case the container has a tradename it needs to be included in sections 3 and 6 of the PL.

In section 6 of the PL the word "micrograms" should be used instead of the abbreviation "µg".

Where an adjuvant or adsorbant is present in a vaccine, section 6 of the PL should include the following or an equivalent statement: "Substance-X is included in this vaccine as an <adjuvant>,<adsorbant>. <Adjuvants> <Adsorbants> are substances included in certain vaccines to accelerate, improve and/or prolong the protective effects of the vaccine".

If the vaccine contains established media as excipients, the same description as given in section 6.1 of the SmPC (e.g. Medium 199 containing vitamins, minerals salts and amino acids), should be used in section 6 of the PL.

Complete information regarding instructions for use, handling and disposal by the user should be included in the PL.

Annex

The Annex provides examples on the appropriate use of the common name, examples how to present the qualitative and quantitative composition as well as on the nature and contents of container in the Smock of vaccines for human use

ATTACHMENT 1 – Examples of common names in SmPC section 1 for novel and combination vaccines

Examples for novel vaccines

Dengue vaccine (rDNA, live)

Ebola vaccine (rDNA, live)

Ebola vaccine (rDNA)

Examples for combination vaccines

Diphtheria, tetanus and pertussis vaccine (adsorbed).

Diphtheria, tetanus and pertussis (acellular, component) vaccine (adsorbed).

Diphtheria, tetanus, pertussis (acellular, component) and hepatitis B (rDNA) vaccine (adsorbed).

Hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed).

Diphtheria, tetanus, pertussis (acellular, component) and haemophilus type b conjugate vaccine (adsorbed).

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA) and poliomyelitis (inactivated) vaccine (adsorbed).

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus type b conjugate vaccine (adsorbed).

ATTACHMENT 2 – Examples of how to present section 2. Qualitative and Quantitative Composition

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus type b conjugate vaccine (adsorbed)

After reconstitution one dose (x ml) contains:

Diphtheria toxoid[1]	not less than x International Units (IU)
Tetanus toxoid[1]	not less than x International Units (IU)
Bordetella pertussis antigens	
Pertussis toxoid (PT)[1]	x micrograms
Filamentous Haemagglutinin (FHA)[1]	x micrograms
Pertactin (PRN)[1]	x micrograms
Hepatitis B surface antigen (HBs)[2,3]	x micrograms
Poliovirus (inactivated) (IPV)	
type 1 (Mahoney strain)[4]	x D-antigen unit
type 2 (MEF-1 strain)[4]	x D-antigen unit
type 3 (Saukett strain)[4]	x D-antigen unit
Haemophilus influenzae type b polysaccharide (polyribosylribitol phosphate, PRP) [3] conjugated to tetanus toxoid as carrier protein approximately	x micrograms

x milligrams Al^{3}+ in total

[1] adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$)

[2] produced in yeast cells (*Saccharomyces cerevisiae*) by recombinant DNA technology

[3] adsorbed on aluminium phosphate ($AlPO_4$)

[4] propagated in VERO cells

Hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed)

One dose (x ml) contains:

Hepatitis A virus <strain> (inactivated)[1, 2]	x ELISA Units (EU)
Hepatitis B surface antigen [3, 4]	x micrograms

x milligrams Al3+ in total

[1]Produced on human diploid (MRC-5) cells.

[2]Adsorbed on aluminium hydroxide, hydrated

[3]Produced in yeast cells *(Saccharomyces cerevisiae)* by recombinant DNA technology.

[4]Adsorbed on aluminium phosphate

Meningococcal group B vaccine (rDNA, adsorbed)

One dose (x ml) contains:

Neisseria meningitidis serogroup B fHbp subfamily A[1,2,3]	x micrograms
Neisseria meningitidis serogroup B fHbp subfamily B[1,2,3]	x micrograms

[1] Recombinant lipidated fHbp (factor H binding protein)

[2] Produced in *Escherichia coli* cells by recombinant DNA technology

[3] Adsorbed on aluminium phosphate (x milligram Al^{3+} in total)

Meningococcal group B Vaccine (rDNA, component, adsorbed)

One dose (x ml) contains:

Recombinant *Neisseria meningitidis* group B NHBA fusion protein [1, 2, 3]	x micrograms
Recombinant *Neisseria meningitidis* group B NadA protein [1, 2, 3]	x micrograms
Recombinant *Neisseria meningitidis* group B fHbp fusion protein [1, 2, 3]	x micrograms
Outer membrane vesicles (OMV) from *Neisseria meningitidis* group B strain NZ98/254 measured as amount of total protein containing the PorA P1.4 2	x micrograms

[1] produced in *E. coli* cells by recombinant DNA technology

[2] adsorbed on aluminium hydroxide (x milligrams Al^{3+} in total)

[3] NHBA (Neisseria Heparin Binding Antigen), NadA (Neisserial adhesin A), fHbp (factor H binding protein)

Measles, mumps and rubella vaccine (live)

After reconstitution, one dose (x ml) contains:

Measles virus[1] <strain> (live, attenuated)	not less than x $CCID_{50}$[2]
Mumps virus[1] <strain> (live, attenuated)	not less than x $CCID_{50}$[2]
Rubella virus[1] <strain> (live, attenuated)	not less than x $CCID_{50}$[2]

[1]produced in < cellular system used for production> cells.

[2]50% cell culture infectious dose.

Human Papillomavirus vaccine (rDNA, adjuvanted, adsorbed)

One dose (x ml) contains:

Human Papillomavirus[1] type 16 L1 protein[2,3,4]	x micrograms
Human Papillomavirus[1] type 18 L1 protein[2,3,4]	x micrograms

[1]Human Papillomavirus = HPV

[2]adjuvanted by AS04 containing:

3-O-desacyl-4'- monophosphoryl lipid A (MPL)[3] x micrograms

[3]adsorbed on aluminium hydroxide, hydrated (Al(OH)3) x milligrams Al^{3+} in total

[4]L1 protein in the form of non-infectious virus-like particles (VLPs) produced by recombinant DNA technology using a Baculovirus expression system which uses Hi-5 Rix4446 cells derived from *Trichoplusia ni*.

Human Papillomavirus Vaccine (rDNA, adsorbed)

One dose (x ml) contains approximately:

Human Papillomavirus1 Type 6 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 11 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 16 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 18 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 31 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 33 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 45 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 52 L1 protein[2,3]	x micrograms
Human Papillomavirus1 Type 58 L1 protein[2,3]	x micrograms

[1]Human Papillomavirus = HPV.

[2]L1 protein in the form of virus-like particles produced in yeast cells (*Saccharomyces cerevisiae* CANADE 3C-5 (Strain 1895)) by recombinant DNA technology.

[3]Adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant (x milligrams Al^{3+} in total).

Pneumococcal polysaccharide conjugate vaccine (adsorbed)

One dose (x ml) contains:

Pneumococcal polysaccharide serotype 1[1,2]	x micrograms
Pneumococcal polysaccharide serotype 4[1,2]	x micrograms
Pneumococcal polysaccharide serotype 5[1,2]	x micrograms
Pneumococcal polysaccharide serotype 6B[1,2]	x micrograms
Pneumococcal polysaccharide serotype 7F[1,2]	x micrograms
Pneumococcal polysaccharide serotype 9V[1,2]	x micrograms
Pneumococcal polysaccharide serotype 14[1,2]	x micrograms
Pneumococcal polysaccharide serotype 18C[1,3]	x micrograms

Pneumococcal polysaccharide serotype 19F[1,4] x micrograms
Pneumococcal polysaccharide serotype 23F[1,2] x micrograms
[1] adsorbed on aluminium phosphate x milligram Al^{3+} in total
[2] conjugated to protein D (derived from non-typeable *Haemophilus influenzae*) carrier protein x micrograms
[3] conjugated to tetanus toxoid carrier protein x micrograms
[4] conjugated to diphtheria toxoid carrier protein x micrograms

Examples for novel vaccines:

Herpes zoster vaccine (rDNA, adjuvanted)

After reconstitution, one dose (x ml) contains:

Varizella Zoster Virus[1] Glycoprotein E antigen[2,3] x micrograms

[1] Varicella Zoster Virus = VZV

[2] adjuvanted by AS01B containing:

plant extract *Quillaja saponaria* Molina, fraction 21 (QS-21) x micrograms

3-O-desacyl-4'-monophosphoryl lipid A (MPL) from *Salmonella minnesota* x micrograms

[3]Glycoprotein E (gE) produced in Chinese Hamster Ovarian (CHO) cells by recombinant DNA technology

Dengue vaccine (rDNA, live)

After reconstitution, one dose (x ml) contains:
Chimeric yellow fever* dengue virus serotype 1 (live, attenuated)** x CCID50***
Chimeric yellow fever* dengue virus serotype 2 (live, attenuated)** x CCID50***
Chimeric yellow fever* dengue virus serotype 3 (live, attenuated)** x CCID50***
Chimeric yellow fever* dengue virus serotype 4 (live, attenuated)** x CCID50***
*Yellow fever vaccine strain 17D-204
**Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).
***CCID50: 50% Cell Culture Infectious Dose.

Ebola vaccine (rDNA, live)

One dose (x ml) contains:
Vesicular Stomatitis Virus expressing glycoprotein GP of Ebola virus <strain>[1] …not less than x CCID50[2]

[1] Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).
[2] CCID50: 50% cell culture infectious dose

Ebola vaccine (rDNA)
One dose (x ml) contains:
Chimpanzee Adenovirus Virus serotype 3 expressing glycoprotein GP of Ebola virus <strain>[1] ….not less than x CCID50[2]

[1] Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).
[2] CCID50: 50%cell culture infectious dose

ATTACHMENT 3 - Examples of entries under SmPC section 6.5 Nature and Contents of Container

Example

0.5 ml suspension in pre-filled syringe (Type I glass) with plunger stopper (chlorobutyl rubber) with or without needle in pack sizes of 5 or 10.

Not all pack sizes may be marketed.

Example

1.0 ml suspension in a vial (type I glass) with stopper (chlorobutyl rubber) with needle, in a pack size of 1.

Example

0.5 ml suspension and 0.5 ml of solution in prefilled syringe (Type I glass) with dual chambers, a plunger stopper (chlorobromobutyl rubber blend), a tip cap (bromobutyl rubber) and a by-pass stopper (bromobutyl rubber), in a pack size of 1.

Example

10ml (20 x 0.5ml doses) suspension in a vial (Type I glass) with stopper (bromobutyl rubber), in a pack size of 1.

Example

1.5 ml of oral suspension in a squeezable tube (polyethylene) fitted with a membrane and a tube cap (polypropylene) in pack sizes of 1, 10 or 50.