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Committee for Medicinal Products for Human Use (CHMP)

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

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

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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 included 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 the other guidelines and documents which are referenced in this document. Applicants are advised to take this guideline into account when submitting new applications for Marketing Authorisation (MA) for vaccines, and may consider it when applying for renewal of, or variations to, existing MAs for vaccines for human use, where the product information is already approved.

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, formulation and use.

Specific guidance on the description of strains for influenza vaccines is provided in the “Guideline on influenza vaccines – submission and procedural requirements” [1]. All other aspects of this guideline on quality aspects included in the product information for vaccines for human use apply to influenza vaccines.

3. Legal basis

This guideline has to be read in conjunction with the introduction and general principles (4th paragraph) of the Annex I to Directive 2001/83 and part I of the said Annex, 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 [3], List of standard terms for pharmaceutical dosage forms, routes of administration, and containers [4], Technical Guide for the elaboration of monographs on vaccines and other immunological human medicinal products [5], Guideline on Excipients in the label and package leaflet of medicinal products for human use [6], 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 [7], Note for guidance on stability testing of new drug substances and products [8], Note for guidance on stability testing of existing drug substances and products [9], Note for guidance on maximum shelf life of sterile products after first opening or following reconstitution [10] and Guideline on declaration of storage conditions: A: in the product information of medicinal products B: for active substances [11].

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

In general, promotional statements such as 'serum-free cells', 'preservative-free', 'latex-free' are not permitted 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 (sero)types the invented name may include the number and/or names of (sero)types present [3].

Strength

The strength should be included where 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 where risk of misadministration of the vaccine exists (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 or combined Standard Terms.

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".

In case of vaccines presented in multidose containers, the appropriate combined Standard Terms of the pharmaceutical form should be used, i.e. <powder and solvent for suspension for injection in multidose container>, <solution for injection in multidose container> or <suspension for injection in multidose container>.

Common name of the vaccine

For vaccines, the international non-proprietary name (INN) is not applicable. To facilitate a harmonised approach for defining a common name, the title of the relevant European Pharmacopoeia monograph should be used, where one exists. However, there may be reasons to deviate from the Ph.Eur. conventions, such as the use of the term 'recombinant' instead of the term 'rDNA'. Although Ph.Eur. [6] requires use of the term 'rDNA' in its monographs for all products derived by recombinant DNA technology, this might not sufficiently distinguish between products of rDNA technology and DNA/RNA vaccines. Deviations from the pharmacopoeial name should be appropriately justified. In cases where there is no European Pharmacopoeia monograph, the stylistics and precedents of European Pharmacopoeia monograph titles should generally be observed [5]. Usually the common name is defined by the infectious

agent 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:

- 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.
- Recombinant: the vaccine antigen is manufactured using recombinant DNA technology. However the word 'recombinant' 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 number of valences and/or names of (sero)types may be included in the common name if appropriately justified. The word "attenuated" should not be included in the common name but should be reflected in section 2, if appropriate.

For vector-based and chimeric vaccines the term "recombinant" should be used. If the strain is replication competent "live" should also be added.

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 below.

For multivalent vaccines containing various (sero)types and/or antigens of a pathogen, all (sero)types and/or antigens 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" (in case of vaccines containing living or replication-competent micro-organisms),
- "Live, attenuated" (in the case of vaccines containing living or replication-competent micro-organisms which have weakened pathogenicity),
- "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 used 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 on the name of active substance(s) concerned.

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 are defined in the "Guideline on excipients in the label and package leaflet of medicinal products for human use". [6] However this list is not exhaustive and applicants need to conduct an assessment of all excipients used. Excipients identified to have an 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 the abbreviations, 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 [4] 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 and/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[1] 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> <and> <12> should appear.

6.3 Shelf life

The shelf-life declaration(s) should be in accordance with the SmPC Guideline [2] and with related guidance documents [8,9,10] addressing the shelf lives of un-reconstituted and reconstituted vaccines as necessary.

The expression of the shelf-life should be in accordance with the current QRD template [7].

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 [8,9,11].

In case appropriate stability data are available which confirm the quality of the vaccine after temporary exposure to temperature conditions outside the recommended storage conditions, this information might be added in section 6.4. The statement should specify the temperature range and maximum duration of temporary storage. 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. These data are intended to guide healthcare professionals in case of temporary temperature excursion only."

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 [2] 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. The appearance of the vaccine before and following reconstitution should be given in section 6.6.

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.

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 they appear 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" [4] 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 [7]. 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 SmPC 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 (recombinant, live)

Ebola vaccine (recombinant, live)

Ebola vaccine (recombinant)

Examples for combination vaccines, where a monograph already exists

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

There may be reasons to deviate from the Ph.Eur. conventions such as the use of the term 'recombinant' instead of the term 'rDNA'. The examples below reflect deviations from the pharmacopoeial name where it was appropriately justified.

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 x micrograms

(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 Al^{3+} 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 [Types 16, 18] (recombinant, 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 9-valent vaccine (recombinant, 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 (recombinant, 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 micrograms3-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 (recombinant, live)

After reconstitution, one dose (x ml) contains:

Chimeric yellow fever* dengue virus serotype 1 (live, attenuated)**	x $CCID_{50}$***
Chimeric yellow fever* dengue virus serotype 2 (live, attenuated)**	x $CCID_{50}$***
Chimeric yellow fever* dengue virus serotype 3 (live, attenuated)**	x $CCID_{50}$***
Chimeric yellow fever* dengue virus serotype 4 (live, attenuated)**	x $CCID_{50}$***

*Yellow fever vaccine strain 17D-204

**Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).

***$CCID_{50}$: 50% cell culture infectious dose.

Ebola vaccine (recombinant, live)

One dose (x ml) contains:

Vesicular Stomatitis Virus expressing glycoprotein GP of Ebola virus <strain>[1] (live)…not less than x $CCID_{50}$[2] or PFU[2]

[1] Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).

[2] $CCID_{50}$: 50% cell culture infectious dose or PFU: plaque forming units

Ebola vaccine (recombinant)

One dose (x ml) contains:

Chimpanzee Adenovirus Virus serotype 3 expressing glycoprotein GP of Ebola virus <strain>[1] ….not less than x $CCID_{50}$[2] or PFU[2]

[1] Produced in < production cells> by recombinant DNA technology. This product contains genetically modified organisms (GMOs).

[2] $CCID_{50}$: 50% cell culture infectious dose or PFU: plaque forming units

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.

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