Product Literature Standard

Contents

1. Introduction

This Standard is meant as a guide for both Applicants when they are creating mock-ups for submission to regulatory authorities, and regulatory authorities when they are assessing mock-ups. This reference is to be used as a joint document between the Veterinary Medicines Directorate (VMD) and the Irish Medicines Board (IMB) (hereafter referred to collectively as the competent authority).

The main body of this standard includes requirements and guidance that are common to both the VMD and the IMB. Separate Annexes have been created that deal with requirements that are specific to the individual competent authorities; Annex A deals with the requirements specific to the VMD and Annex B deals with the requirements that are specific to the IMB.

This Standard brings together existing requirements into one bespoke document for a convenient reference rather than setting new requirements for product literature.

This document has been agreed with the assessors of the VMD and the IMB as well being discussed with industry representatives.

2. Definitions

The following definitions are used throughout this document and, where possible, have been taken from existing definitions in EU Directive 2001/82/EU as amended by 2004/28/EC and 2009/9/EC[1]:

- **Immediate Packaging** – The container or any other form of packaging that is in direct contact with the Veterinary Medicinal Product (VMP) e.g. vials, ampoules, bottles, blister packs, etc. Immediate packaging does not include capsules which are administered as part of the product.
- **Outer Packaging** – The packaging into which is placed the immediate packaging e.g. cartons, boxes, packets, etc.
- **Label** – Information on the immediate packaging or outer packaging.
- **Package Leaflet** – The leaflet that contains information for the user that accompanies the VMP.
- **Product Literature** – Consists of the labelling for the immediate packaging, labelling for the outer packaging and the package leaflet.
- **Summary of Product Characteristics (SPC)** – Contains the information on the VMP as developed during the course of the assessment process.
- **Mock-Up** – A flat artwork design in full colour, presented so that, (following cutting and folding, where necessary), it provides a full size replica of both the outer and immediate packaging so that the three dimensional presentation of the label text is clear. This may also be referred to as a "paper copy" or a "computer generated version".
- **Specimen** – A sample of the actual printed outer and inner packaging materials and package leaflet. This may also be referred to as the "sales presentation".

[1] http://ec.europa.eu/health/files/eudralex/vol-5/consol_2004/dir_2001_02-dir_2004_28-cons_en.pdf

3. Legal Requirements

Labelling of VMPs has a legal basis in EU Directive 2001/82/EU as amended by 2004/28/EC and 2009/9/EC ("The Directive"). The following are the relevant extracts from this directive together with an explanation for their meaning. Please note this is not a comprehensive list of requirements relating to product literature as detailed in The Directive. For example, Title V of The Directive sets out the particulars to be included on the immediate/outer packaging and the package leaflet but is not repeated here as the requirements are detailed under chapter 4 "General Requirements".

Article 12(3) point (l):

"The file shall be submitted in accordance with Annex I and shall contain, in particular, the following information:

…a summary in accordance with Article 14 of the product characteristics, a mock-up of the immediate packaging and the outer packaging of the veterinary medicinal product, together with the package leaflet, in accordance with Articles 58 to 61…"

This sets out the requirement to submit a draft SPC and mock-ups of the product literature with the submission of an application for a marketing authorisation (MA).

Article 25(2):

"The competent authority shall take all necessary measures to ensure that information concerning the veterinary medicinal product, and in particular the labelling and package leaflet, is in conformity with the summary of product characteristics approved when the marketing authorisation was granted or subsequently."

This requires that competent authorities assess and approve the product literature to be in accordance with the approved SPC.

Article 26(1):

"The marketing authorisation may require the holder to indicate on the immediate packaging and/or the outer wrapping and the package leaflet, where the latter is required, other particulars essential for safety or health protection, including any special precautions relating to use and any other warnings resulting from the clinical and pharmacological trials prescribed in Article 12(3)(j) and in Articles 13 to 13d or from experience gained during the use of the veterinary medicinal product once it has been marketed."

This sets out the provision to include additional information on the product literature where required.

Article 30 point (e):

"The authorisation shall also be refused if, after examination of the documents and particulars listed in Articles 12 and 13(1), it is clear that:

…the labelling or the package leaflet proposed by the applicant does not comply with this Directive…"

This sets out the provision to refuse an MA if the product literature is not in conformance with The Directive.

4. General Requirements

4.1 Scope

The Marketing Authorisation Holder (MAH) is responsible for the immediate packaging, outer packaging and any package leaflet of an authorised VMP as set down in the MA. The competent authority must approve all product literature and any subsequent change to the text (including its font and layout) usually requires a variation. However, small changes to the labelling that have no effect on the legally required statements and warnings, or their legibility, may be made without the need for a variation. For example, a change to a barcode would not necessitate a variation. The inclusion of the pharmacopoeial grades of active substances or excipients on packaging is no longer required and is being phased out. Therefore, if the only change to be made to a label concerns the deletion of statements such as BP and Ph. Eur., it may be made without the prior approval of the competent authority. Changes to the colouring of the product literature constitute a variation as any potential effect on legibility needs to be assessed. Similarly, a variation is generally required when proposing a new corporate design of packs, a new container type/size, use of different colours or changes in the layout. If you are in any doubt as to whether a variation is needed, please contact a member of the General Assessment Team at the VMD or vetinfo@imb.ie at the IMB. For products that are joint labelled in UK and IE (see section 5.1), variations to change the country specific information need only be submitted as a variation to the relevant country.

To ensure that an application for a new MA, a renewal or a variation to an existing MA, satisfies the criteria set out in The Directive, the product literature is assessed and authorised. The labelling requirements apply to the immediate packaging, outer packaging and the package leaflet of the retail product literature. The labelling of the cartons in which the product literature is packed for distribution to wholesalers and retailers (shipping packs) is **not** assessed. Datasheets, including Material Safety Data Sheets (MSDSs), are also **not** assessed or approved by the competent authority.

The templates provided in all EEA languages on the EMA Website (http://www.ema.europa.eu/) reflect the particulars which must appear on the labelling and package leaflet of VMPs according to The Directive. They will help to ensure that the information appears as intended by The Directive, and to ensure consistency in the information provided across a number of different VMPs and across Member States.

When using these templates, reference should be made to relevant Community Guidelines, Quality Review of Documents group (QRD) Guidance and the "Annotated QRD Template", which provides detailed guidance on how to complete each section and which can be found on the EMA Website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000185.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058002d9b0

Having used the templates provided, MAHs/applicants will still need to format the resulting text into the relevant full colour mock-ups or specimens of the label and package leaflet. These mock-ups should only include the information that is included on the QRD template with no deviation from the text agreed during a procedure (with the exception of the additional national requirements listed below). Although permitted, the use of the QRD headings on immediate and outer packaging is not obligatory, only the agreed text is obligatory. However, essential headings that clearly convey meaning (e.g. withdrawal period) must be included. Should any deviations be required from the approved QRD text, the applicant should draw them to the attention of the assessor and provide a sound justification for their omission/amendment. Such instances will be reviewed on a case-by-case basis.

The EMA website also contains other useful documents for use when submitting mock-ups to competent authorities and therefore applicants may wish to consult this website in conjunction with this standard:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000204.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058002d4ee&jsenabled=true

4.2 Submission of Mock-Ups

Mock-ups may be submitted in either electronic format, i.e. computer-generated, or hard copy. It should be noted that electronic copies do not always print out as clearly as hard copy mock-ups, particularly for small labels and small font text. Applicants may choose to submit printed mock-ups that are clearer to read. If electronic copies are not legible, applicants will be asked to submit printed hard copy mock-ups. They must be submitted as actual size or, if not, the dimensions must be provided, e.g. large containers may have reduced size mock-ups provided an indication of the actual size is given. Labels for small containers should be provided as actual size so that legibility and readability can be assessed but, in addition, a scaled up copy should also be supplied to make it easier for the competent authority to mark any required changes. An indication of the font size of the text as it will appear on the marketed labels should also be provided. If applicants wish to deviate

from this procedure, they must first discuss it with the relevant assessor, who will deal with each request on its merits.

There may also be occasions where the competent authority requests to see specimens of the actual labels, for example when it is considered that readability may be of concern. It is anticipated that this will be a rare occurrence and you will be contacted if this is required.

The competent authority is happy to accept and approve text instead of full colour mock-ups for pack sizes that are not marketed. If the MAH then decides to market the product they must first obtain competent authority's approval of the finalised mock-ups. The assessment of these mock-ups will be dealt with via a variation application (Type IB C.II.6), which will attract the normal fee.

4.3 Fonts for Electronic Source Documents

If the fonts are not embedded in the PDF document, the reviewer at the competent authority may find that fonts and symbols do not appear as in the original document. Agencies cannot guarantee the availability of any fonts except Times New Roman, Arial and Courier, and fonts supported in the Acrobat product itself. Therefore, all additional fonts used in the PDF files should be embedded to ensure that those fonts would always be available to the reviewer. When setting options for font embedding, choose options that indicate that (1) all fonts should be embedded and (2) fonts should not be subsetted. Embedding fonts will increase the size of the PDF file. Information about type font and style can be found under 6.1.

4.4 Labelling

The label must provide all the following information on the immediate packaging if practical to do so and should conform to the particulars in the SPC. These requirements are also outlined in Title V, Articles 58 and 61 of The Directive. The information is listed as a guide to the normal order of priority, in which it must appear on the container. However, for certain products the order of priority may need to be modified to ensure that the most important warnings for those products are immediately apparent. There is no need for any outer packaging or package leaflet if you are able to fit all of the required information on the immediate packaging (Title V, Article 61 of The Directive). The use of flag or concertina labels on the immediate packaging is acceptable and is one way to provide sufficient space for the required statements and warnings. The requirements below are also reflective of requirements set out in the QRD templates; however, information highlighted in **bold** are specific national requirements for the competent authority.

- The name of the veterinary medicinal product followed by its strength and pharmaceutical form. The common name shall appear if the medicinal product contains only one active substance and its name is an invented name. The name of the veterinary medicinal product should appear on the product literature exactly as it appears in section 1 of the SPC.
- The name and quantity of each active substance and of any excipient if this is specified in section 2 of the SPC.
- The method and route of administration (if not immediately apparent).
- The batch number.
- The expiry date.
- The words “For animal treatment only” and for prescription only products (those classified as POM-V or POM-VPS by the VMD and/or POM by the IMB) also the words, “To be supplied only on veterinary prescription”.
- The contents by weight, volume or number of dose units.
- The marketing authorisation number (Vm xxxxx/xxxx for the VMD and VPA xxxxx/xxx/xxx for the IMB).
- The MAH and distributor (if this is different to the MAH) name and address. This should include the name or corporate name and permanent address or registered place of business of the MAH and, where appropriate, of the representative designated by the MAH.
- The name and address of the manufacturer responsible for batch release.
- A suitably labelled space to record discard date (if relevant). The following statement should be included on the package leaflet (where this exists) if there is an in-use shelf life “When the container is broached/opened for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the carton should be discarded should be determined. This discard date should be written in the space provided.”
- The target species.
- **The distribution category. For all products, the distribution category must appear in a box e.g.:**
  VMD categories: **POM-V**, **POM-VPS**, **NFA-VPS**, **AVM-GSL**
  IMB categories: **VPO**, **VPO-1**, **POM**, **POM(E)**, **PS**, **LM**, **CAM**
- The words “Keep out of the reach and sight of children”.
- Storage instructions as they appear on the SPC.
- The in-use shelf-life (if appropriate).
- For food-producing species, the withdrawal period for each species and for the various foodstuffs concerned (meat and offal, eggs, milk, honey). The withdrawal period must always be shown, even if it is zero days/hours, for products intended for food producing species. Also all contra-indications relating to food consumption should be stated.
- Any warning specified in the MA (target species or user or environment) considered to be essential for that product (e.g. penicillin hypersensitivity

warning / mineral oil self injection). All user warnings appear together and separate from the target species warnings under defined subheadings, i.e. “User Warnings”.
- Disposal advice.
- Full indications.
- Dosage instructions.
- Contra-indications.
- Further information required in the MA.
- If the product is one that requires a dose to be specified for the animal being treated, a space for this. Where all of the information cannot be included on the immediate packaging, an empty space only needs to be provided for the prescribed dose on the outer packaging.
- Adverse reactions with the statement “If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.”

4.5 Immediate and Outer Packaging

If it is not practical to fit all of the information above on the immediate or outer packaging then at least the following information should be included. In addition to this information, the immediate and outer packaging must also have as much information as reasonably practical from the above while still being able to be easily read. The requirements below are also reflective of requirements set out in the QRD templates; however, information highlighted in **bold** are specific national requirements for the competent authority.

- The name of the veterinary medicinal product followed by its strength and pharmaceutical form (the addition of strength and pharmaceutical form may not be applicable to immunological products). The pharmaceutical form according to the full “Standard Terms” has to be mentioned on the outer package only; however, the pharmaceutical form must be stated as part of the name on the immediate label.
- The name and quantity of each active substance, (and of any excipient that is known to have a recognised action or effect).
- The method and route of administration (if not immediately apparent).
- The batch number.
- The expiry date.
- The words “For animal treatment only” and if appropriate, “To be supplied only on veterinary prescription”.
- The contents by weight, volume or number of dose units.
- The marketing authorisation number.

- The MAH and distributor (if this is different to the MAH) name and address. This should include the name or corporate name and permanent address or registered place of business of the MAH and, where appropriate, of the representative designated by the MAH.
- The target species.
- **The distribution category. For all products, the distribution category must appear in a box.**
- The words “Keep out of the reach and sight of children”.
- Storage instructions as they appear on the SPC.
- The in-use shelf-life (if appropriate).
- The withdrawal period(s) or contra-indications relating to food consumption.
- Any warning specified in the MA (target species or user or environment) considered to be essential for that product (e.g. penicillin hypersensitivity warning / mineral oil self injection). All user warnings appear together and separate from the target species warnings under defined subheadings, i.e. “User Warnings”.
- Disposal advice.
- For immunological products, information on the indication(s). In case of space limitation a shorter statement for the indication is acceptable e.g. For active immunisation against Porcine Circovirus.
- The words “Read the package leaflet before use”.

4.6 Package Leaflets

If all the information cannot be provided on the immediate container then the outer packaging must contain all the information as detailed under 4.4. If this is not reasonably practical, a package leaflet must be enclosed in the package (Title V, Article 61 of The Directive). The package leaflet must provide all the information listed under 4.4 and should relate solely to the VMP with which it is included. However, consideration may be given to allowing joint package leaflets for product ranges (see 5.3 below). It is expected that the information included in the package leaflet should conform to the particulars in the SPC and that all user warnings appear together under defined subheadings, i.e. “User Warnings” (see 6.5 below). The immediate packaging and outer packaging must refer to the use of the package leaflet and must carry as a minimum the information set out under 4.5 together with as much information as reasonably practical from the information under 4.4. Additionally, the date on which the package leaflet was last approved should also be included if the package leaflet is not being approved for the first time.

4.7 Ampoules and Small Single-Dose Containers

In the case of ampoules or other small unit dose forms, where the container cannot have the required information in a size that can be easily read, the following information must be shown on the immediate packaging. On a case-by-case basis, this minimum information could be considered for other containers (e.g. small multidose containers over 50 ml). As above, the outer packaging must contain all the information under 4.4 and if this is not practical then a package leaflet must be supplied. These requirements are also outlined in Title V, Article 59 of The Directive.

- The name of the veterinary medicinal product followed by its strength and pharmaceutical form (the addition of strength and pharmaceutical form may not be applicable to immunological products). Short terms for the pharmaceutical form according to "Standard terms" published by the Council of Europe may be used in case of space limitation.
- The name and quantity of the active substance.
- Contents by weight, volume or by number of doses.
- The route of administration (if not immediately apparent).
- Withdrawal period(s).
- The batch number.
- The expiry date.
- The words "For animal treatment only".

4.8 Blister Packs or Strips

For blister packs and strips, where it is not possible to include all of the required information, the following information must be included. Again, the outer packaging must contain all the information under 4.4 and if this is not practical then a package leaflet must be supplied.

- The name of the veterinary medicinal product followed by its strength and pharmaceutical form. Short terms for the pharmaceutical form according to "Standard terms" published by the Council of Europe may be used in case of space limitation.
- The name of the MAH (full or short name).
- The batch number.
- The expiry date.
- The words "For animal treatment only".

4.9 Small Containers other than Ampoules and Small Single-Dose Containers

In the case of small immediate containers, such as vaccine vials or very small volume spot-on products, containing a single dose, on which it is impossible to give the particulars mentioned under 4.5 or even 4.7, then the immediate packaging must include at least the batch number and expiry date and as much of the other information stated under 4.4 as possible. All information under 4.4 must still appear on the outer packaging (or in a package leaflet if this is not possible). This should only occur in exceptional circumstances.

4.10 Additional Points for Consideration

In addition to the above points, the following should be considered when creating mock-ups and submitting them to the competent authority.

- Space available on labels should be considered during the assessment process (both by applicants and assessors). The text included in the QRD template must also reflect the size of the label. Justified deviations from the required text must be discussed and agreed during the assessment process and not during the review of mock-ups
- All packaging must be presented in a legible manner that is clearly and easily understood by those involved in the supply and administration of the product. The critical information should appear in as large a font as is possible to maximise legibility. Please see further information in Chapter 6.
- In order that the user of the medicine can easily see all the necessary information in one place, all information should be placed on either the immediate or outer packaging or package leaflet.
- Packaging may not refer to websites; however, it is acceptable to include a telephone number and/or an e-mail address.
- The use of clear diagrams and pictograms in addition to wording, to reinforce the correct use of the product, is encouraged.
- The MA number should be presented as “Vm” and not “VM” for products authorised by the VMD and as “VPA” and not “Vpa” for products authorised by the IMB and should appear on all product literature where possible. The exceptions to this are when a label has been designated as a ‘small immediate label’ or for blisters/strips and it is not feasible to include this information. Such instances will be reviewed on a case-by-case basis.
- The name of the VMP should exactly match that specified on the SPC. This name should be kept together with the description of the product in English. For example the name of the product should be kept together with the pharmaceutical form (either after or directly under the name of the product). Other items must not be included in the name, but copyright/trademark

symbols such as ® or © are permissible. Letters in the product name should not be replaced with symbols and the orientation of the name should be considered to ensure it is presented as an integrated item. For multi-lingual labels, the preference is that the name in English should appear together with the pharmaceutical form and strength (i.e. as stated in section 1 of the SPC) and not separated.

- The competent authority has agreed to move towards including mg/ml, mg/g, etc. in the naming of VMPs rather than %w/v, %w/w, etc. This is in line with the rest of Europe who prefer mg/ml and can insist on it. However, there is no legal requirement to move away from %w/v and if a company particularly wanted to retain %w/v or %w/w to be consistent with other products or reference products, we would not force them to change.

5. Specific Requirements

5.1 UK/IE Joint Labelling

The country specific information should be presented in a similar way to the example below:

UK Only Vm xxxxx/xxxx POM-V	**IE Only** VPA xxxxx/xxx/xxx POM

For Ireland, the package leaflet should state the method of sale and supply in full. Please note that this is the VMD and IMB's preference on how the country specific information should be presented; however, other forms are acceptable. For example, if there is a lack of space, "UK only" and "IE only" do not need to be included if it is obvious which country the information relates to (e.g. under UK/IE distributor).

The words "to be supplied only on veterinary prescription" do not necessarily need to appear in each box. If wording is common across both countries, they can appear once outside the box.

5.2 Inclusion of Addresses on Product Literature

The name and address of the MAH and distributor (if this is different from the MAH) should always be included on the product literature.

The applicant should ensure that the UK distributor holds a wholesale dealer's authorisation (WDA) that permits distribution of the type of product concerned if the distributor is not the MAH or the holder of a manufacturing authorisation.

It is acceptable for a company to include the name of a local representative instead of the distributor on the product literature. However, the company should confirm the name and address of the distributor for the competent authority's records. In most cases, it is expected that the local representative will be the same as the MAH and/or distributor.

The name and address of the manufacturer for the batch release of the product should also be stated on the package leaflet. If this manufacturer is the same as the

MAH, this should be clearly indicated on the package leaflet. Equally, if this manufacturer differs from the MAH, this too should be clearly indicated.

Where several company names and addresses are included, the role of each should be clearly identified.

The addresses included on the product literature may be shorter than the address on the SPC. Where there is limited space, it may be acceptable to omit the postal address from the product literature; however, this should be considered on a case-by-case basis in consultation with the competent authority.

Where an address is given, the country name must be included in the address if the company is located outside the country concerned. Addresses of companies within IE should also include the county.

5.3 Product ranges

There should be a separate SPC and product literature for each strength and pharmaceutical form of a medicinal product. On a case-by-case basis national competent authorities or the European Commission may however agree to allow the use of combined package leaflets for different strengths and/or different pharmaceutical forms (e.g. tablets and capsules), for instance where achieving a recommended dose necessitates a combination of different strengths, or when the dose varies from day to day depending on the clinical response. Simple reference to other strengths and pharmaceutical forms of the same medicine is always possible if necessary for the therapy. For instance, referring to a different strength, or referring in the package leaflet of a tablet which is unsuitable for dogs weighing less than 5 kg to the availability of an oral solution which is authorised for use in this subgroup of target species.

In accordance with the QRD decisions on stylistic matters in product information, a combined printed package leaflet can only be acceptable if **all** the following 3 conditions are met:

- Posology in the SPC / package leaflet foresees 2 dosages (e.g. a high induction dose followed by lower maintenance dose or different dosages depending on the size of the animal).
- Package leaflets are completely identical, except for the few strength-specific details.
- A combined package leaflet does not cause confusion for the user of the veterinary medicine.

The applicant must submit their request for a combined package leaflet in advance, together with a justification/rationale. A decision to allow this will be taken on a case-by-case basis.

5.4 Strength and Total Content

In some cases the packaging may need to contain information on both the quantity per unit volume and on the total quantity per total volume. The total quantity per total volume can be particularly important for safety reasons for injectable products and other medicines available in solution or suspension.

Different strengths of the same medicinal product should be expressed in the same manner: for example 250 mg, 500 mg, 750 mg, 1000 mg and NOT 1 g. Trailing zeros should not appear (2.5 mg and NOT 2.50 mg). The use of decimal points (or comma) should be avoided where these can be removed (i.e. 250 mg is acceptable whereas 0.25 g is not). For safety reasons it is important that micrograms is spelt out in full and not abbreviated. However, in certain instances where this poses a practical problem which cannot be solved by using a smaller type size then abbreviated forms may be used, if justified and if there are no safety concerns.

5.5 Route of Administration

This should be as written in the SPC according to the standard terms. In principle only standard abbreviations may be acceptable (i.v., i.m., s.c.,) and then only on small immediate packaging. Other non-standard routes of administration should be spelled out in full. Some routes of administration will be unfamiliar to users and may need to be explained within the package leaflet. This is particularly important when medicinal products are made available for administration by the animal owner.

5.6 Multi-Dose Containers

For multi-dose containers of quantities **greater than,** or **equal to** 50 ml, the in-use shelf-life and a suitably labelled space for either the date of first use or discard date must always appear on the label of the immediate container.

For multi-dose containers of **less than** 50 ml, the expectation is that a suitably labelled space for the discard date will be included on the label of the immediate container. The in-use shelf life should ideally be included on the label of the immediate container. Where an in-use shelf life is included, the suitably labelled space may be used to record a date of first use rather than a discard date.

If you consider that there is insufficient space to include these important statements, you must first consider whether or not you have fully optimised the layout, font size etc. of the label. If necessary, to ensure the legibility of important warnings, the scale of company logos should be reduced. If, despite efforts to improve the available space on the label, you are convinced that the inclusion of these statements will render more important warnings illegible, you should submit to the competent authority a mock-up of the proposed label to illustrate this. If the competent authority is satisfied that the inclusion of these statements is impractical, then you may include the statements on the outer package instead.

5.7 Blister Pack Presentations

For blister pack presentations it is important that the particulars remain available to the user up to the point at which the last dose is removed. Often it will not be possible to apply all the information over each blister pocket, consequently where a random display of the information is proposed it should frequently appear across the pack. In all cases it will be acceptable to apply the batch number and expiry date to the end of the blister strip. If technically possible, applying this information to both ends of each strip should be considered. Where a unit-dose blister presentation is proposed all the information required for blister packs must appear on each unit dose presentation. In addition, blister foils should be printed to ensure maximum legibility of the information using a sufficiently large font. Colour for the text and the font style, should be chosen carefully as the legibility of the text on the foil is already impaired due to the nature of the material. Where possible, non-reflective material or coloured foils should be considered to enhance the readability of the information presented and the correct identification of the medicine.

5.8 Expiry Dates

In order to avoid confusion on whether the expiry date means that the product can be used until the end of the stated month, or used by the end of the preceding month, the expiry date of your product should be clearly expressed. For example, the labels or package leaflet could include the phrase “Do not use after the expiry date stated on the label”. Alternatively the following formats for the expiry date of the labels could be used:

- Expiry date: DD/MM/YY
- EXP: DD/MM/YY
- EXP: end MM/YY
- Use by end MM/YY

Where the shelf life of the product is less than 12 months then a DD/MM/YY format should be used for the expiry date.

Expiry dates, and batch numbers, may be printed, embossed or engraved onto labels. However, it is essential that, irrespective of the method of application, these are clear and easy to find. The expiry date (and batch number) should be included on all immediate and outer packaging. If they are overprinted onto the final printed packaging this should be stated when submitting the mock ups.

It is illegal to sell, supply or use a product after its stated expiry date.

5.9 Multilingual Packs

All labels and package leaflets must be in English. However, they may contain other languages provided that the information given is identical, the requirements of the competent authority are respected and the legibility of the warnings in English is not compromised.

The principles of this standard also apply to multilingual packs and the use of these packs will not be approved if this compromises the readability in any way. English text should always be kept together. The competent authority will only assess the content of the English text on the product literature but it is expected that content in other languages should be equivalent to the English text.

If an MAH wishes to introduce a multilingual pack for an already authorised product, they must submit the appropriate variation to the competent authority in order to have the change approved.

5.10 Disposal Advice

Disposal advice for product literature should be included in accordance with the wording from section 6.6 of the SPC. However, it may be necessary to include special requirements for disposal and any environmental warnings as agreed during assessment.

5.11 Prescription Only Distribution Categories

All product literature should contain the following statement: “To be supplied only on veterinary prescription” for products in the distribution category POM-V or POM-VPS (products authorised by the VMD) and/or POM (products authorised by the IMB).

5.12 Veterinary Homeopathic Remedies

Homeopathic veterinary medicinal products should follow the same labelling requirements as any other veterinary medicinal product and specifically:

- The labels, in clearly legible form, should include the words 'homeopathic medicinal product for veterinary use'.
- Clear mention of the words 'homeopathic veterinary medicinal product without approved therapeutic indications'.
- The scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the pharmacopoeia. If the homeopathic veterinary medicinal product is composed of more than one stock, the labelling may mention an invented name in addition to the scientific names of the stocks.
- Name and address of the registration holder and, where appropriate, of the manufacturer,
- Method and, if necessary, route of administration.
- Expiry date
- Pharmaceutical form.
- Contents of the sales presentation.
- Special storage precautions, if any.
- Withdrawal period(s) or a statement if the product is contraindicated for animals intended for human consumption.
- Target species.
- A special warning if necessary for the medicinal product.
- Manufacturer's batch number.
- Registration number.
    - In the UK, a registered product will have a registration number preceded by the symbol Vh on its product literature, e.g. labels; this offers users a clear guarantee that the VHR has been assessed and approved in accordance with the instructions on the product literature.
    - In IE, a registered product will have a registration number in the following format: HoVR 01/001, where HoVR represents homeopathic veterinary registration, 01 is the number allocated to the company and 001 is the product number.

5.13 Labelling of Small Homeopathic Remedies Containers

As specified in the Directive all the required particulars must appear on either the container or the package; where the container itself is not more than 50 ml, reduced labelling may be applied. In this case the minimum labelling requirement for small containers of registered homeopathic products should be as follows:

- Clear mention of the words ‘Homeopathic veterinary medicinal product’ as part of the required statement ‘Homeopathic veterinary medicinal product without approved therapeutic indications’.
- The scientific name of the stock(s) followed by the degree of dilution, supplemented by an invented name where required.
- The route of administration.
- The registration number specified in the certificate of registration.
- The name of the holder of the registration certificate.
- The contents of the presentation, specified by weight, volume or number of doses.
- The manufacturer’s batch number and expiry date.
- The withdrawal period, if relevant

The outer packaging must in all circumstances contain all of the labelling particulars, including those already stated on the small container.

6. Readability

The following is extracted and reproduced from the "Guideline on the Readability of the Labelling and Package Leaflet of Medicinal Products for Human Use" [2]. There is no specific guideline for Veterinary Medicinal Product; however, the principles of the human guideline should be followed. Product literature can be designed in any style an MAH wishes although it should not compromise legibility as detailed below (e.g. use of contrasting colours, large pictures with small text, small text with large amounts of white space, etc.).

When taking into account legibility, consideration should be given to removing text from immediate and outer packaging and placing the complete set of information in a package leaflet in line with the requirements laid out under 4.4, 4.5, 4.6, 4.7, 4.8 and 4.9. If, despite considering the requirement laid out in these sections, all of the required information cannot be included in the immediate and outer packaging without compromising legibility, additional removal of text or abbreviations may be permitted. However, this will only be permitted in exceptional circumstances and where all the space available has been utilised (removal of company logos, full use of white space, conversion of a multilingual pack into English only, etc). It would usually be expected that the following does not need to appear on the immediate or outer packaging if there is insufficient space:

- Disposal advice.
- Full indications (although abbreviated indications may be required).
- Dosage instructions.
- Contra-indications.
- Further information required in the MA.

6.1 Type Font and Style

Choose a font which is easy to read. Stylised fonts which are difficult to read should not be used. It is important to choose a font in which similar letters/numbers, such as "i", "l" and "1" can be easily distinguished from each other.

The widespread use of capitals should not be used. The brain recognises words in written documents by the word shape, so choose lower case text for large blocks of text. However, capitals may be useful for emphasis.

[2] http://ec.europa.eu/health/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf

Do not use italics and underlining as they make it more difficult for the reader to recognise the word-shape. Italics, however, should be used for Latin terms (e.g. when referencing bacteria organisms or citing correct nomenclature).

6.2 Type Size – Package Leaflet

For the package leaflet, the type size should be as large as possible to aid readers. It is recommended that a type size of 9 points, as measured in font 'Times New Roman', not narrowed, with a recommended space between lines of at least 3 mm, is used as a minimum. It is advised that a type size of 8 points, as measured in font 'Times New Roman', not narrowed, with a recommended space between lines of at least 3 mm, is used as an absolute minimum in exceptional circumstances. If the space available has been fully utilised and the necessary information still cannot be included in the package leaflet without compromising legibility, consideration can be given to reducing the font size further.

6.3 Type Size – Product Literature other than the Package Leaflet

The particulars appearing on the label of all medicinal products is recommended to be printed in characters of at least 7 points (or of a size where the lower case "x" is at least 1.4 mm in height), leaving a recommended space between lines of at least 3 mm. In particular the information presented on small packs will need careful consideration so that the text is presented in as large a type size as possible to reduce the likelihood of treatment error. If the space available has been fully utilised and the necessary information still cannot be included on the product literature without compromising legibility, consideration can be given to reducing the font size. It is considered that the font size on small pack sizes should be an absolute minimum of 4.75 points and this should only be used in exception circumstances in consultation with the competent authority. Consideration should be given to removing text rather than reducing type size.

6.4 Design and Layout

The use of "justified" text (that is text aligned to both left hand and right hand margins) should in principle not be used.

Line spaces should be kept clear. The space between lines is an important factor influencing the clarity of the text. As a general rule the space between one line and the next should be at least 1.5 times the space between words on a line, where practical.

Contrast between the text and the background is important. Factors like paper weight, colour of the paper, size and weight of the type, colour of the type and the paper itself should be considered. Too little contrast between the text and the background adversely affects the accessibility of the information. Therefore, background images should in principle not be placed behind the text since they may interfere with the clarity of the information making it harder to read.

A column format for the text can help the reader navigate the information. The margin between the columns should be large enough to adequately separate the text. If space is limited a vertical line to separate the text may be used. Related information should be kept together so the text flows easily from one column to the next. Consideration should be given to using a landscape layout which can be helpful to users of the veterinary medicine. Where a multilingual leaflet is proposed there should be a clear separation between the different languages used; all the information provided in each language should be assembled together.

Applicants and MAHs should make best use of the space available to ensure that the important information is clearly mentioned on prime spaces on the outer and immediate packaging, presented in a sufficiently large type size. Company logos and pictograms (if accepted) may be presented, where space permits, on the outer packaging and on immediate packaging, provided they do not interfere with the legibility of the mandatory information.

Use of a large type size will be appropriate, although other factors may also be important in making the information legible. Consideration should be given to the line-spacing and use of white space to enhance the legibility of the information provided. For some small packs it may not be possible to present all the critical information in the same field of view. The use of any innovative technique in packaging design to aid in the identification and selection of the medicinal product is encouraged. It is also encouraged where space is at a premium.

Colours should be chosen to ensure a good contrast between the text and the background to assure maximum legibility and accessibility of the information. Highly glossy, metallic or reflective packaging should be avoided, as this affects the legibility of the information.

Different colours in the name of the product are discouraged since they may negatively impact on the correct identification of the product name. The use of different colours to distinguish different strengths is strongly recommended.

Similarity in packaging which contributes to treatment error can be reduced by the judicious use of colour on the pack. The number of colours used on packs will need careful consideration as too many colours could confuse. Where colour is used on

the outer pack it is recommended that it is carried onto primary packaging to aid identification of the medicine.

Where a multilingual outer and/or immediate packaging is proposed there should be a clear separation between different languages where space permits.

6.5 Headings

Headings are important and can help users of the veterinary medicine to navigate the text if used well. Therefore, bold type face for the heading or a different colour, may help make this information stand out. The spacing above and below the headings should be consistently applied throughout immediate packaging, outer packaging and the package leaflet. Same level headings should appear consistently (numbering, bulleting, colour, indentation, font and size) to aid the reader.

The use of multiple levels of headings should be considered carefully, as more than two levels may make it difficult for readers to find their way around the product literature. However, where complex information has to be communicated multiple levels of headings may be needed.

Using lines to separate the different sections within the text can also be helpful as a navigational tool.

6.6 Print Colour

Accessibility is not only determined by print size. Characters may be printed in one or several colours allowing them to be clearly distinguished from the background. A different type size or colour is one way of making headings or other important information clearly recognisable and can help to facilitate navigation in the text.

The relationship between the colours used is as important as the colours themselves. As a general rule dark text should be printed on a light background. But there may be occasions when reverse type (light text on a dark background) could be considered to highlight for instance particular warnings. In such circumstances the quality of the print will need careful consideration and may require the use of a larger type size or bold text.

Similar colours should not be used for the text and background as legibility is impaired.

6.7 Paper

The paper weight chosen should be such that the paper is sufficiently thick to reduce transparency which makes reading difficult, particularly where the text size is small. Glossy paper reflects light making the information difficult to read, so the use of uncoated paper should be considered. Make sure that when the package leaflet is folded the creases do not interfere with the readability of the information.

6.8 Use of Symbols and Pictograms

The use of images, pictograms and other graphics to aid comprehension of the information is encouraged, but these should not include any element of a promotional nature. Symbols and pictograms can be useful provided the meaning of the symbol is clear and the size of the graphic makes it easily legible. They should only be used to aid navigation, clarify or highlight certain aspects of the text and should not replace the actual text. Evidence may be required to ensure that their meaning is generally understood and not misleading or confusing. If there is any doubt about the meaning of a particular pictogram it will be considered inappropriate. Particular care will be needed when symbols are transferred or used in other language versions of the package leaflet.

ANNEX A: VMD Requirements

The VMD has created its own national SPC/QRD templates to aid applicants in considering the requirements for product literature. These templates can be found under templates on the application forms page of the VMD website at http://www.vmd.defra.gov.uk/pharm/forms_new.aspx and should be used for the submission to the VMD of all new national applications for MAs, Exceptional MAs, Parallel Imports (MAPIs) not based on mutually recognised products and Extensions.

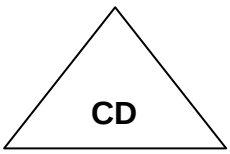
Immediate and Outer Packaging

If it is not practical to fit all of the information above on the immediate or outer packaging then, in addition to the requirements set out in 4.5, the following should appear on the immediate and outer packaging for products authorised by the VMD:

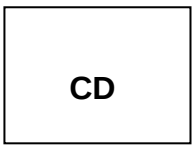
- The words “Keep the container in the outer carton”. This statement should be included on all product literature if an outer carton is used. This does NOT only refer to products which need to be protected from light. However, if the smallest labels cannot contain this information due to lack of space, this may be acceptable.

Controlled Drugs

VMPs containing controlled drugs are authorised as POM-V. Products containing controlled drugs in Schedule 2 or 3 of the Misuse of Drugs Regulations 2001 will be clearly identified with “CD” either in a triangle (preferable) or a box (see diagrams below) and the relevant schedule detailed on their labels.



(Sch 2)



(Sch 2)

Warnings for Horse Products

Warnings such as the following are not considered necessary on the SPC or product literature of VMPs.

“Horses intended for racing and competition should be prevented from racing or competing when in need of treatment and horses which have been recently treated should be dealt with according to local requirements. Appropriate precautions must be taken to ensure compliance with competition regulations.”

The VMD considers that it is the veterinary surgeons responsibility to ensure that any horse treated with a VMP would comply with competition rules and that warning such as this are not a target animal safety or efficacy issue.

Warnings such as these should not be introduced onto the SPC and/or product literature and, if they are already included, should be removed at the earliest opportunity, e.g. during a variation or renewal procedure.

Anthelmintics

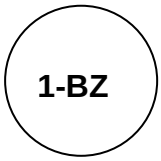
A voluntary labelling scheme has been introduced in the UK for all manufacturers of sheep anthelmintics to enable easy identification of the anthelmintic chemical group by prescribers and farmers. This has the potential to facilitate efforts to delay the development of anthelmintic resistance. The proposal outlined below refers to anthelmintics for use in sheep and cattle only but companies may wish to adopt the labelling proposal for anthelmintics for use in other species.

The symbol to be used and included on the product literature is a circle design with appropriate colour and anthelmintic group code. The examples of which are included below.

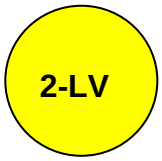
The location of the symbol on the outer pack should be such that it is easy for the prescriber and farmer to locate. The symbol should be repeated on the immediate packaging where possible and on the package leaflet. It is permissible for the symbol on package leaflet to be monochrome. A symbol minimum diameter of 10mm is suggested for the outer packaging (this size can be scaled up for larger packs). Manufacturers can also display the anthelmintic group in ways in addition to, but not instead of, the symbol (e.g. flash across front corner of outer packaging).

No symbol should be required for narrow spectrum anthelmintics e.g. closantel. For example, closantel/mebendazole combination drench would display the 1 BZ symbol, closantel only drench would display no symbol.

These symbols are intended to provide a simple method of identifying the class of anthelmintic chemicals that the active substance in the product belongs to.

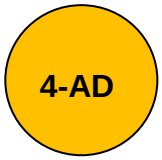


Benzimidazoles



Levamisole

Macrocylic Lactones



Amino-acetonitrile Derivatives

The VMD would prefer that these changes are included as part of another variation but, if not, we will accept them as free-of-charge notifications. Such notifications will only be accepted if the inclusion of the symbol does not compromise legibility, or result in the movement of information from the immediate packaging to the outer packaging or from the outer packaging to a package leaflet. The VMD will check the notifications they receive and in cases of issues (for example legibility) a variation and fee may be required.

Exceptional Marketing Authorisations

The Regulations allow a product to be authorised in specific and restricted circumstances, without all the comprehensive data on therapeutic effects, which is normally required. In such cases the package leaflet and labels must make it clear to the person prescribing or using the product that, in certain specified respects, the particulars available concerning the medicinal product are incomplete. For further information please refer to VMG Note 2.

Products with Exceptional Marketing Authorisations, in addition to being subject to the normal requirements for labelling for veterinary medicines, are required to carry the following information on their product literature:

- A clear statement that the product does not have a full Marketing Authorisation and to highlight the area of “weakness”. For example, “This is a Limited Marketing Authorisation. A full set of supporting efficacy data is not available for this product”.

- The statement “All suspected adverse reactions and any suspected lack of efficacy should be reported to (company pharmacovigilance phone number and address)”.
- The statement “Further information on this product and its supporting data can be found on http://www.vmd.defra.gov.uk/ProductInformationDatabase/”.

The first of these statements should wherever possible appear on the primary pack label. Where this is not possible this statement, together with the other statements should appear on package leaflet if there is one, where there is no package leaflet the statements should appear on the outer carton.

Animal Test Certificates (ATCs)

An ATC imposes conditions regarding labelling. These conditions require that the containers and outer packages of products must be labelled clearly and indelibly in accordance with the general labelling rules for products with MAs. For small containers, alternative words should be discussed with the VMD. Where trials are being conducted according to a blind design, these rules will be relaxed to the extent necessary to allow for this. A package leaflet is required if there is insufficient space on the label to include all relevant text. For Type A and B ATCs, label and package leaflet text should be submitted for approval, and the approved labels and package leaflet must be used for the trial. For Type S ATCs, the applicant will be required to submit a statement of user and target species safety warnings to appear on the label/leaflet, but otherwise it is the responsibility of the ATC holder to ensure that the labelling/leaflets conform to requirements.

As a general rule the VMD will expect labels to contain the following minimum information in English:

- The words "For Veterinary Clinical Trial Use Only".
- Name or other designation of the product.
- Quantity of product.
- Any restrictions on use.
- Expiry date and, if appropriate, in-use expiry date.
- Directions for use specific to the trial including dosage, frequency, duration, method and route of administration.
- Contra-indications, warnings and precautions, and special instructions for handling and storing the product.
- Instructions for disposal (in most cases, these should state that any unused product and containers should be returned to the trial sponsor).

- If to be used in species used to produce food (including horses, rabbits and pigeons) either the specified withdrawal period or the words "Not to be Used in Animals for Human Consumption".
- Name and address of ATC holder and ATC number.
- The manufacturer's batch number.
- A unique code/number identifying the individual container, where appropriate (e.g. where the identity of the products used in the trial are blinded).

For authorised veterinary medicinal products, the approved labelling may be used, providing it is in English, but a small overlabel should indicate any amended directions/warnings, the ATC number and the words “Veterinary Clinical Trial Use Only” to ensure accountability in line with GCP requirements. If any of the above is likely to cause difficulties, particularly in respect of blind trials, please contact the VMD for guidance. There are suggested proformas for the labelling of materials to be used in a clinical trial on the VMD website:

http://www.defra.vmd.gov.uk/pharm/forms_new.aspx

You will need to adapt these as appropriate to take account of the nature of individual studies.

Dedicated Dispensing Containers (Guidance for MAHs, Veterinary Surgeons and Suitably Qualified Surgeons)

The authorised packaging of a product usually consists of either immediate packaging labelled with all of the required information and warnings, or outer packaging containing a labelled inner container and a package leaflet. Some distributors additionally provide empty, partly-labelled packs, such as envelopes, wallets or cartons for use with specific products. These are intended to be used by veterinary surgeons to supply the dispensed medicines. These product-specific (or manufacturer-specific) dispensing containers offer a convenience for the veterinary surgeon. For the company marketing the product, they help to promote the name of the product or the authorisation holder.

Where such dedicated dispensing containers are supplied to the veterinary surgeon separately from the authorised pack, they are not subject to the requirements applied to labels and other packaging texts for authorised products and are not approved by the VMD. Instead, the usual requirements for labelling of dispensed medicines will apply. Dispensing of VMPs into these containers is the responsibility of the veterinary surgeon. However, if the dedicated dispensing containers are enclosed within the authorised packaging, then these are considered to form part of the authorised packaging and subject to scrutiny and approval by the VMD.

Veterinary medicines, which fall under the distributional category POM-VPS, may be supplied by Suitably Qualified Persons (SQPs). SQPs operating at registered merchants cannot supply only part of the contents of an immediate container, for example 200 ml of drench from a 500 ml pack. However, for certain medicines they may supply a number of immediate containers removed from a larger package as long as package leaflets are provided, for example two vials of vaccine from a pack of 24. In order to clearly identify these veterinary medicines it is intended that the following statements will be introduced into the product literature and SPC:

Carton/Package Label
“Individual units of this product may be supplied but each must be accompanied by a package leaflet.”

SPC, section dealing with the packaging:
“Each carton/package contains a sufficient number of package leaflets so that individual units may be supplied by Suitably Qualified Persons.”

ANNEX B: IMB Requirements

For Nationally Authorised Immunological Products Only

If a product is classified as LM, the following warning is required:

“Prior to first time use on a farm, it is strongly recommended that the advice of a veterinary practitioner is sought”.

Exceptional Marketing Authorisations

The Regulations allow a product to be authorised in specific and restricted circumstances, without all the comprehensive data on therapeutic effects, which is normally required. In IE, the Department of Agriculture, Fisheries and Food (DAFF) is responsible for authorisation under this provision. Information on labelling requirements for products authorised under exceptional circumstances can be obtained from DAFF.

Products for use in Veterinary Clinical Trials

In IE, the Department of Agriculture, Fisheries and Food (DAFF) is responsible for authorisation of veterinary clinical trials. Information on labelling requirements for products authorised for use in veterinary clinical trials can be obtained from DAFF.

Dedicated Dispensing

Whilst not a requirement, it is the IMB’s preference that mock-ups of all dispensing materials intended to be supplied by a marketing authorisation holder (MAH) to facilitate the dispensing of their product by a registered veterinary practitioner, pharmacist, the holder of an animal remedies merchant’s licence (responsible person) or a person entered in the ‘companion animal medicine sellers register’ (registered person), should be submitted to the IMB for review and approval.

For new products, mock-ups of dispensing materials should be submitted at the time of submission of mock-ups of other product livery (immediate/outer packaging and package leaflet). For existing products, mock-ups of new or existing dispensing materials should be submitted by way of a variation application (with accompanying fee).

Note that in the case of joint labelling procedures between the IMB and the VMD where dispensing materials are not enclosed within the authorised packaging but are to be supplied independently of the authorised packaging, such mock-ups will be assessed independently by the IMB only.

The following points should be considered by the MAH before submitting mock-ups of dispensing materials to the IMB for review and approval.

- Dedicated dispensing materials are considered as 'supplementary packaging materials' and are not to be used as a replacement for official packaging materials.
- The choice of whether or not to use dispensing materials (wallets/cartons etc.) rest with the prescribing veterinarian, the pharmacist or the responsible/registered person dispensing the product and who is responsible for ensuring that all relevant information concerning the product being dispensed is provided to the animal owner.
- Responsibility for the assessment of the suitability/adequacy of any form of dispensing material (in terms of child resistance/user safety, manufacturing materials etc) rests with the person dispensing the product and will not be considered by the IMB in the context of assessing such mock-ups.
- All text must be of an adequate font size to ensure legibility (as for all other product literature).
- Only approved information (i.e. information included in the SPC and/or labelling/leaflet texts) agreed during the product application procedure may be included on the dispensing materials.
- Promotional or marketing statements will not be approved and therefore should not be included.
- Space requirements for dispensing information (such as name & address of veterinary practice, date of dispensing, client details etc) should be considered by the applicant.
- The legal category of route of sale/supply and VPA number must be included.
- The text to be included on the dispensing material should normally include the QRD text approved for immediate packaging units as a minimum.