Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

EMEA/CMDv/123457/2008 ed. 01-final
London, 28 November 2008

LABELLING & PACKAGING OF VETERINARY MEDICINAL PRODUCTS

CONCLUSIONS AND RECOMMENDATIONS

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CONTENTS

1 Introduction

IFAH-Europe, a veterinary pharmaceutical industry representative organisation, organised in April 2006 a workshop in Prague to discuss with European regulatory authorities ways to make labelling and packaging requirements more cost effective in view of significant problems that had been identified with prohibitive cost of small print runs. Industry indicated that reducing packaging costs could enhance the availability of veterinary medicines in smaller markets.

As a follow-up to this workshop CMD(v) at the initiative of EMEA carried out a survey, aiming to establish the view of the Member States on proposals made by IFAH-Europe. The survey was finalised in December 2006 and the results revealed that some proposals were immediately acceptable to all Member States whilst the majority met resistance from one or more Member States.

IFAH-Europe presented in April 2007 a priority list for the outstanding proposals. Realising that changes could not materialise, unless there was consensus among all Member States, CMD(v) set up an ad hoc group in July 2007, with the aim to:

- categorise the issues brought forward;
- identify the decision makers for each proposal;
- make recommendations for resolving issues within the remit of CMD(v);
- prepare recommendations from CMD(v) to HMA, the European Commission and industry.

In October 2007 Member States received a second questionnaire, specific to the proposals they were objecting to. As a result Member States not only explained their position, but also re-evaluated and changed it on occasion. All Member States including Iceland, Liechtenstein and Norway responded. Furthermore, a meeting with the QRD group was organised in March 2008 with a view to harmonise the product literature templates used at MRP/DCP and at centralised procedure level.

This document lists CMD(v)'s conclusions on IFAH-Europe's proposals for labelling and packaging which:

- have been accepted by all Member States;
- are not acceptable to certain or all Member States;

and provides recommendations on resolving outstanding issues.

The reasons why certain proposals cannot be accepted, including the legal background and the responsible body at national level are specified in Annex I of this document.

Abbreviations used in this report are listed in Annex II.

2 Accepted proposals

2.1 Multilingual mock-up using 3x English language as standard mock-up

CMD(v) agreed to request by default mock-ups containing three times the English language text for dossier submission, to obtain an impression of the space required for text for three different languages. In situations where more than 3 languages are envisaged, it is advised to present the worst case scenario mock ups e.g. smallest packsize.

2.2 CMD(v) template for Product Information

Templates for Product Information in all official EU languages as well as Icelandic and Norwegian have been developed and are available on the CMD(v) website since December 2007. These templates also help to prevent differences between language packs of Member States sharing common languages, as relevant to:

- Dutch Belgium/the Netherlands
- French Belgium/France/Luxembourg
- German Austria/Belgium/Germany/Liechtenstein/Luxembourg
- Greek Cyprus/Greece
- Swedish Finland/Sweden

It is recommended that applicants contact the RMS and CMS during a procedure to ensure harmonised texts if they wish to have combined packs.

CMD(v) trusts that this also fulfils IFAH-Europe's proposal for a special mechanism to resolve same language issues.

2.3 Agreement on Product Information during MRP/DCP

The Best Practice Guide for MRP, the BPG for DCP and the BPG for RMS have been adapted in order to reflect the fact that all efforts have to be made during the procedure to agree on harmonised labelling and leaflet.

The following paragraphs have been added:

- *The Applicant and RMS should make sure that during the procedure, the complete SPC, labelling and leaflet have been agreed, taking into account that in some Member States multi-lingual labels are necessary and that in some cases the Applicant seeks to have combined labels in more than one Member State. In such cases, a space restriction might exist and a solution has to be sought trying to take into account the legal requirement for harmonisation and the national legal requirements the safe use of veterinary medicinal products.*

- *After issuing the Marketing Authorisation, any changes to the product information (final SPC, leaflet or labelling) should be considered as a variation.*

2.4 Changes to Directive 2001/82/EC

CMD(v) could support the proposals for amendments to Directive/2001/82/EC as indicated in section 4.3 of this document.

3 Partly accepted and not accepted proposals

3.1 *Lot* and *Exp*

Member States accept that *batch number* is replaced by *Lot,* and *expiry date* by *Exp* on any pack size. However, the use is restricted to small pack sizes only in:

- Germany (pharmaceuticals), Italy and Poland for *Lot* and *Exp*
- the Czech Republic for *Lot*
- Norway for *Exp.*

For more detailed information see Annex I.

3.2 Replacing *for animal treatment only*

Member States cannot accept the replacement of *for animal treatment only* on smaller packs by *ad us vet* or *veterinary use* (translated into the national language) nor by mentioning the target species. However, it should be noted that some Member States have in their official language a very short wording for *for animal treatment only*.

Member States support the proposal to change the Directive to shorten the text (see also section 4.3). The proposal to extend the scope of article 59 to include provisions for blister packs and all small immediate packs, is also supported.

For more detailed information see Annex I.

3.3 Limit the "blue box" information to that agreed for the Centralised Procedure.

Member States agree to limit the blue box information to that agreed for the Centralised Procedure, with the exception of Germany (pharmaceuticals).

For more detailed information see Annex I.

3.4 Flexible interpretation of single-dose

Member States may accept a flexible interpretation of single-dose, so as to standardise and minimise information appearing on a single-dose container and its outer packaging, with the following exceptions: Germany, Italy, Slovenia and Slovakia. In Italy the distinction for any minimisation of information is based on volume and not on dose.

For more detailed information see Annex I.

3.5 Flexible definition of small vial

Member States, except Austria and Germany, can accept a small vial being at maximum 50 ml as for the Centralised Procedure. In Norway this applies in case of multilingual labelling only.

For more detailed information see Annex I.

3.6 Foreign language

Member States would not support an amendment of article 61 of the Directive to allow the possibility to use an alternative mutually-agreed language (other than the official language of the Member State) for the immediate and secondary packaging. Also not supported is the proposal to exempt applicants from translation into a national language if the expected product sales are below an agreed minimum threshold.

3.7 Over-stickering

Over-stickering of a foreign language pack with a sticker in the national language can be accepted subject to conditions by most Member States, but not by Bulgaria, Finland and Luxembourg. It is noted that over-stickering should be performed under GMP.

For more detailed information see Annex I.

3.8 Use of pictograms on certain labels as a replacement for text

Member States do not accept text to be replaced by pictograms (e.g. target species).

3.9 Pharmaceutical form in the name of the veterinary medicinal product

Member States agree that it is not necessary to include the pharmaceutical form in the product name as long as it appears close to the product name on the package.

3.10 Administered by veterinarians only

Member States do not support the proposal to change in article 61 *administered only by veterinarians* into all *prescription-only* products.

4 Recommendations

4.1 To industry

For the IFAH-Europe proposals that were not acceptable to all Member States the reasons and responsible actors are outlined in the annex to this document. CMD(v) recommends industry to contact the indicated actors for the proposals they wish to pursue.

Furthermore CMD(v) recommends industry to make use of the accepted proposals and looks forward to increased availability of medicines in particular for smaller markets.

4.2 To HMA

A number of IFAH-Europe proposals have been accepted by a majority of the Member States. However, even if there is just one disagreeing Member State, this may result in difficulties during Mutual Recognition and Decentralised Procedures and negate the efforts made. It is therefore recommended that each Head of Agency reconsiders the negative responses provided by their Agency to issues accepted by most other Member States, as most of the proposals require changes to national legislation

CMD(v) suggests that the HMA-task force on legislative changes should take note of the results in this document.

4.3 To the European Commission

As a result of the questionnaires undertaken, the CMD(v) has acquired a good view on the ideas and practical implementation of EC legislation by the National Competent Authorities. CMD(v) can support the following proposals for amendments to Directive/2001/82/EC. The European Commission is requested to take note of these when reviewing the Directive.

Article 58

Amend the introductory wording to add at the end of the 1st paragraph "...and be compatible with the requirements of European tri-lingual labelling." When space permits, it should also be possible to have more than 3 languages on the label to support availability in small Member States.

The requirement to provide space for the prescribed dose to be indicated should be removed as this is not necessary for products only to be administered (or prescribed) by veterinarians.

Article 59

Extend the scope to blister packs and small immediate packaging. Rephrase paragraph 1 on ampoules to stipulate 'small immediate packaging', so that it is in line with Article 55(3).

Delete paragraph 3 and amend the particulars listed in paragraph 1, in line with the proposals for short term implementation.

Paragraph 3 states that the route of administration and the words 'for animal treatment only' should be put in the national language on the outer and immediate packaging of the Medicinal Product.

Regarding "for animal treatment only" the Member States agree that a direct translation of these words can be too long and therefore alternative easily understandable wording may be acceptable. Due to specific translations of the proposals, it might be helpful not to specify the wording exactly but to make clear that the product is intended for animals only.

The scope of Article 59 should be widened by the inclusion in paragraph 2 of a definition of what constitutes a small immediate pack. It might be more correct to have a definition based on volume, instead of based on single dose or ampoule.

Article 61
To allow the possibility to use multi-lingual labels with a minimum amount of information, most of which may not need translating (e.g. name of product, manufacturer, exp, lot, MA number), provided that full information is provided in the official language(s) in the leaflet.

4.4 To the EMEA
CMD(v) recommends harmonising templates for product information for Centralised procedures, Decentralised procedure and Mutual recognition procedure and all guidance regarding labelling. CMD(v) is therefore looking forward to continue good collaboration with the EMEA-CMD(v) secretariat and the QRD-Group.

5 Final conclusion

The CMD(v) hopes that the indicated actors would follow up on the recommendations of this document and looks forward to receiving feedback on the progress made.
The CMD(v) trusts that as a result of this harmonisation exercise hurdles have been removed and will be removed for the marketing of products in smaller markets and looks forward for industry to increase the availability of veterinary medicinal products in the near future.

Annex I Reasons for non acceptance

Ad 3.1 The use of *Lot* for batch number and *Exp* on all pack sizes

	Reason	Legal reference	Responsible for change
CZ	We accept the use of "Exp" for expiry date on all packs. We accept the use of "Lot" on the small immediate packaging only (following rules done in appendix IV for QRD templates). Non-acceptance of the use of "Lot" on the other than small immediate packaging is the result of joint opinion based on agreement between Czech human and Czech veterinary agencies.	The opinion was presented to the applicants.	Institute for the State Control of Veterinary Biologicals and Medicaments (Ústav pro státní kontrolu veterinárních biopreparátů a léčiv)
DE bvl	Required by law	German Drug Law para 10 (1) No. 4 and 9	German legislator
IT	legal	Batch number and expiry date required to be in Italian language by Decree 193/2006 (basic law on VMP), with the exception of small immediate packaging	Director General to initiate process for modification of Decree

NO	Lot: Yes Exp.: No.(only small labels)	Readability and NO legislation : the expiry date should be spelled out in clear text. In our experience NO/SE/DK/FI have had multilingual packaging and it has not been a big problem to include national language	
PL	We accept „Lot" and "EXP" on small immediate packaging only. When the "Lot" and "EXP" is used we require on the outer labeling: "Nr serii (Lot)" and Termin ważności (EXP).This follows rules done in Appendix IV for QRD Templates. We do not want to change the rules because the abbreviations are not clear for all people administering the VMP.		Ministry of Health

Ad 3.2. Ad us vet

	Yes/No	If no, reason	Legal reference	Responsible for change
CY	No			Registrar of Council of VMPs
DE bvl	Yes for English version No for German version	Required by law	German Drug Law para 10 (8) in conjunction with para 10 (5) No. 1	German legislator
EL	No	Demand of our Ministerial Decision 282371/FEK 731 B/16-6-2006, article 57(4)	Directive 2001/82 as amended, article 58(4)	National Organisation for Medicines (EOF) Veterinary Section
ES	No	Directive 2001/82 as amended.- Art 58	Directive 2001/82 as amended.- Art 58	
FR	No	Not used in French (not understandable)		
IE	No	The phrase 'For animal treatment only' is required by national legislation	Schedule 2, European Communities (Animal Remedies) (No. 2) Regulations 2007, SI 786/2007	
IS	Not as a general rule. “Ad us vet.” is not a phrase generally known by the public. The Nordic countries have for a very long time used the extension “vet.” after the name of the product, to clearly identify medicinal products for animal use. This could become a general rule. Also, it is possible to replace “for animal treatment only” with a short word - “Dýralyf” which means “Veterinary medicinal product”. Clearly, it would also be of major benefit if some symbol could replace this text. The symbol would not have to be an animal. Could be “Noah’s Ark” or any other symbol. The same symbol would have to be stated in all PILs with an explanation. It should be easy to implement such a symbol			

	Yes/No	If no, reason	Legal reference	Responsible for change
IT	No	legal	The only allowed sentence for smaller packs, including ampoules or blister**,** is ”per uso veterinario” in Italian language (Decree 193/2006 - basic law on VMP),	Director General to initiate process for modification of Decree
NL	No	National legislation does not allow this.	Diergeneesmiddelen-regeling; article 62, f; The label should mention the wording: ‘diergeneesmiddel’ or ‘geneesmiddel voor diergeneeskundig gebruik’. Further article 72, 1; The label should be in Dutch, readable, not to erase and understandable.	Ministerie van LNV (Landbouw, Natuur en Voedselkwaliteit).
NO	No (In products administered by veterinarians only “ad us. vet.” could be considered acceptable in multilingual labels (injectables).	The use of the shorter term: “for animals “(til dyr) is generally accepted for all pack sizes. For very small immediate packing Units (e.g. spot-on products) the phrase could be replaced by mentioning of target species (or mutually agreed pictograms)	NO and EU law and Directives The phrase “for animals” is written in the NO legislation. For most of the other issues the basic requirement of readability /national language is the essential part. The EU requirements seem in general to be much less flexible than national ones!?	On case by case basis the NoMA can make exemptions from general requirements
PT	No	It is not understandable by all people administering the VMP	Decreto Lei Medicamentos (VMP National provisions – labelling must be in Portuguese)	Government
SE	No	It can not be guaranteed that all users understand this text.	The information vital to the user should be in the national languages, Swedish.	
SI	No	In the legislation it is clearly stated that	Rules on labelling and package	The Minister for health in accordance with

	Yes/No	If no, reason	Legal reference	Responsible for change
		it should be "FOR ANIMALS ONLY"	insert for veterinary medicinal products	the Minister for Agriculture, Forestry and Food. Comment: The Agency is competent for proposing new legislation to the Minister and we have already prepared the first draft of the labelling rules. It is our intention to implement as many simplifications as possible especially those which will be agreed upon in the CMDv.
UK	No	For very small packs (e.g. spot-on products, blister packed tablets with only a small number of tablets per strip), in the UK it is already possible to omit the phrase “For animal treatment only” from the immediate packaging. But these words must appear on the outer packaging or package leaflet in accordance with UK and EU legislation. For larger, but still small packs, the words “For animal treatment only” are a legal requirement in the UK. However, if an alternate EU agreed pictogram were to become available then this could be incorporated into the annual review of the UK legislation. The words “ad us. Vet.” is not considered to be widely recognised and as such could not be accepted. Immunologicals: For vials we do accept the replacement “for animal treatment only”, but only in exceptional circumstances (liquid nitrogen glass vials etc)		Director of Authorisations

Ad 3.2 Veterinary use (translated into the national language)

	Yes/No	If no, reason	Legal reference	Responsible for change
DE bvl	Yes for English version No for German version	Required by law	German Drug Law para 10 (8) in conjunction with para 10 (5) No. 1	German legislator
DE pei	No	Not foreseen in law	German Regulation for Veterinary Vaccines § 35	German legislator
IE	No	As for 'ad us vet'		
LV	No			
NL	No	National legislation does not allow this.	Diergeneesmiddelen-regeling; article 62, f; The label should mention the wording: 'diergeneesmiddel' or 'geneesmiddel voor diergeneeskundig gebruik'. Further article 72, 1; The label should be in Dutch, readable, not to erase and understandable.	Ministerie van LNV (Landbouw, Natuur en Voedselkwaliteit).
NO	cfr.supra			
PL	No	The sentence "For animal treatment only" (translated into Polish) is required according to the directive. We accept "ad use vet" in case of the small packs.	Directive 2001/82	Ministry of Health
SE	No	The sentence "veterinary use" dose not have the same meaning as "For animal treatment only" as several products are handled by the animal owners, farmers and healthcare professionals rather than veterinarians.	The sentence "For animal treatment only" is required according to the directive.	
SI	No	same as 'ad us vet'		
UK	No	As for 'ad us vet'	UK and EU law	Director of Authorisations

Ad 3.2.3 Mentioning the target species

	Yes/No	If no, reason	Legal reference	Responsible for change
CY	No			Registrar of Council of VMPs

CZ	No	Mentioning all target species is not efficient that there are more than 4 species. I this case proposed change does not make sense.		Institute for the State Control of Veterinary Biologicals and Medicaments (Ústav pro státní kontrolu veterinárních biopreparátů a léčiv)
DEbvl	No	Required by law	German Drug Law para 10 (8) para 10 (5) No.1	German legislator
EL	No	Demand of our Ministerial Decision 282371/FEK 731 B/16-6-2006, article 57(4)	Directive 2001/82 as amended, article 58(4)	National Organisation for Medicines (EOF) Veterinary Section
ES	No	Directive 2001/82 as amended.- Art 58	Directive 2001/82 as amended.- Art 58	
FR	No	The meaning is not the same		
IE	No	As for 'ad us vet'	Schedule 2, European Communities (Animal Remedies) (No. 2) Regulations 2007, SI 786/2007	
IT	No	legal	Target species required to be in Italian language by Decree 193/2006 (basic law on VMP), but not obligatory on small immediate packaging.	Director General to initiate process for modification of Decree
LV	No			
NL	No	National legislation does not allow this.	Diergeneesmiddelen-regeling; article 62, f; The label should mention the wording: 'diergeneesmiddel' or 'geneesmiddel voor diergeneeskundig gebruik'.	Ministerie van LNV (Landbouw, Natuur en Voedselkwaliteit).
NO	cfr supra			
PL	No	The sentence "For animal treatment only" (translated into Polish) is required according to the directive. We accept "ad use vet" in case of the small packs. We accept "ad use vet" in case of the small packs.	Directive 2001/82	Ministry of Health
PT	No	Safety reasons – not sufficiently emphasised that the VMP is intended for vet use		
SI	No	same as 'ad us vet'		
SK	No, it is not acceptable.	Because we want to spare space and sometimes number of animals is bigger.	Slovakian Law for Veterinary Medicines Par.53 (1c)	
UK	No	As for 'ad us vet'		Director of Authorisations

Ad 3.3 Blue box

	Reason	Legal reference	Responsible for change
DE bvl	National legislation	German Drug Law	German legislator
DE pei	Required by law	German Regulation for Veterinary Vaccines § 35 (2	German legislator

Ad 3.4 Single dose

	Reason	Legal reference	Responsible for change
DE bvl	The German Drug Law has no special requirements for single dose containers except for ampoules.	German Drug Law para 10 (8)	German legislator
DE pei	No special requirements for labels of single dose containers except for ampoules, requirements only for outer package	German Regulation for Veterinary Vaccines § 35 (5) and (6)	German legislator
IT	legal	In Italy the distinction for any minimisation of information is based on volume and not on dose.	Director General to initiate process for modification of Decree
SI	Comment: the single dose container is the one which contains only one dose. However, not only ampoules can be labelled as small containers. Perhaps there was a slight misunderstanding.		As for B 2.5
SK	No special requirements for labels of single dose containers except for ampoules, requirements only for other types of inner packaging.	Slovakian Law for Veterinary Medicines Par.24(6)	Ministry of Health and ISCVBM

Ad 3.5 Flexible definition of small vial

	Yes/No	If no, reason	Legal reference	Responsible for change
DE bvl	No	Required by law	German Drug Law para 10 (8)	German legislator
DE pei	No	Defined by law with 10ml	German Regulation for Veterinary Vaccines § 35 (5)	German legislator

Ad 3.7 Over-stickering conditions

	Reason	Legal reference (if applicable)
AT	We would allow under the following circumstances: -GMP requirements are met, -only allowed for MA, -only in exceptional circumstances, that means to avoid, lack of alternative products on the market -we are informed in advance about delivery of products which do not comply wit the authorised text on package materials If permanent we would prefer a variation and have multilingual texts on outer Package and or Package-insert Over-stickering often leads to questions from wholesalers, veterinarians or animal owners	GMP regulation MA authorisation: Labels are part of the MA and therefore should not be different to license
BE	Yes, but only in rare cases and on case by case basis. The overstickering must be done under GMP-conditions and if the stickering is done in Belgium, the manufacturer will need an authorisation according to our Royal Decree (14/12/06) and has to have a qualified person.	
EE	Yes, if the veterinary medicinal product is required to be administrated by veterinary surgeon only or in case the actual or expected use of veterinary medicinal product is less than 1000 packages in a year.	
EL	The answer is Yes, but GMP requirements must be fulfilled. This should also be mentioned in our official authorization license.	
ES	We could accept this proposal in a case by case basis. Of course it should be permanent. GMP requirements must be fulfilled. It is only possible in exceptional circumstances.	
IT	The sticker should contain in Italian language all the information foreseen for the product. Additional languages on the package are allowed	
NL	Allowed in rare cases on a case-by-case basis. Overstickering should be conducted to GMP. Overstickering might never lead to less information on the label; all requested information should be present on the label clearly and readable without exception.	
PT	Normally no. In special cases we do authorise it but not as a rule (case-by case). We would allow it only if duly justified and only under certain conditions (namely if GMP requirements are met).	
SE	Not acceptable as a common practice, however this may be approved on a case by case. It should be motivated from MAH and samples of the labelling should be provided upon request prior to the decision. Comment: Responsible body for taking a decision is normally our Department of Inspections	

Ad 3.7 Member States that cannot allow over-stickering:

	Position	Reason	Legal reference (if applicable)
BG	No	Bulgarian veterinary legislation does not allow over-stickering.	Regulation 62/09/05/2006.
DE BVL	No	Due to law the particulars must be given using indelible characters. Only for justified cases allowed on provision that the sticker cannot be removed without damaging the first print and all information foreseen for the product is given	German Drug Law para 10 (1)
DE pei	No	Due to law only permanent particulars are allowed, but for justified individual cases exceptions to the obligation to give particulars in German language are possible	German Regulation for Veterinary Vaccines § 35 (1) and (8)
FI	No	not allowing stickers has nationally been seen a way to prevent counterfeit medicines. No change of policy is foreseen	
LU	No		

Annex II Abbreviations

BPG	Best Practice Guide
BVL	The Federal Office of Consumer Protection and Food Safety (Germany)
CMS	Concerned Member State
CMD(v)	Coordination Group for Mutual Recognition and Decentralised Procedures
DCP	Decentralised Procedure
EC	European Community
EU	European Union
EMEA	European Medicines Agency
GMP	Good Manufacturing Practice
HMA	Heads of Medicines Agencies
MAH	Marketing Authorisation Holder
MRP	Mutual Recognition Procedure
PEI	Paul Ehrlich Institut (Germany)
QRD	Quality Review of Documents
RMS	Reference Member State
VMP	Veterinary Medicinal Product

AT	Austria	IT	Italy
BE	Belgium	LI	Liechtenstein
BG	Bulgaria	LT	Lithuania
CY	Cyprus	LU	Luxembourg
CZ	Czech Republic	LV	Latvia
DE	Germany	MT	Malta
DK	Denmark	NL	Netherlands
EE	Estonia	NO	Norway
EL	Greece	PL	Poland
ES	Spain	PT	Portugal
FI	Finland	RO	Romania
FR	France	SE	Sweden
HU	Hungary	SI	Slovenia
IE	Ireland	SK	Slovakia
IS	Iceland	UK	United Kingdom