



HAI EUROPE RESPONSE

Amsterdam, 28 May 2009

HAI Europe Response to the EMEA Document on the Expression of Strength of Medicines

This response has been prepared by Health Action International (HAI) Europe. HAI Europe is a non-profit, growing, European network of consumers, public interest NGOs, health care providers, academics, media and individuals with over 25 years experience in representing the voice of civil society, and poor and marginalised people in medicines policy debates.

Our authority rests on our integrity and independence from commercial and political party interests, our research excellence and evidence-based advocacy.

- HAI Europe promotes increased access to essential medicines, the essential medicines concept and the rational use of medicines.
- HAI advocates for greater transparency in all aspects of decision making around pharmaceuticals, for example, by reducing industry secrecy and control over important clinical data.
- HAI promotes the rational use of medicines; that all medicines marketed should meet real medical needs; have therapeutic advantages; be acceptably safe and offer value for money.
- HAI works for better controls on drug promotion and the provision of unbiased and independent information for prescribers and consumers.

Summary

Thank you for the opportunity to comment on the document “QRD Recommendations for the expression of strength in the name of centrally authorised human medicinal products”.

Medication errors are frequent in health care and confusing labelling is one important cause. Medication errors are particularly serious in children, but are also important in other age groups though often with fewer medical consequences. Children also lack suitable dosage forms and therefore there is a frequent need to dilute products. With these challenges in mind, we propose the following:

In the 6th paragraph of page 2/5, the draft proposal makes valuable steps towards ensuring a standardisation even though it is only to be used prospectively and for centrally approved medicines. However, due to a difference in opinion in the group preparing the document, the option of allowing one of two expressions have been recommended for some pharmaceutical forms that are for single use.

Single forms may have to be diluted or divided, mainly for children, but also for other patients (e.g. not all patients receive Garamycin 80 mg/2ml). When calculating a dose of, for example, 0,23 mg, the calculation of volume to be withdrawn is more complicated if the ratio is presented as 6 mg/3 ml instead of 2 mg/ml. Using percent (%) as strength would be even more difficult. For this reason we strongly recommend the same principle of labelling strength in single dose preparations (mg/ml) as multi-dose preparations, i.e. mg/ml as part of name, even if the volume is less than 1 ml. We would have preferred that the total amount should be expressed only as the total volume. However, due to the reports of serious overdosing in adults, we agree that the total amount in the container should be added as x mg/y ml, but not as the only way to express the strength, and be displayed less prominently than mg/ml. Our proposed table is attached.

Mg/ml as part of the name raises awareness of different concentrations of the same product (Xylocain 5 mg/ml and 10 mg/ml). Using mg/ml as a standard expression of strength in the name provides continuity in this crucial aspect of product labelling, as companies discontinue and change package size.

Single dose products of other formulations, than injections in small children, can be partially used, and therefore mg/ml should also be used to express strength in solutions for oral use, inhalation, etc. For single dose powders and granules, the total amount should be the most prominent value and mg/g should still be easy to find, preferably on the label. If not possible, the strength in mg/g should be prominent at least in the Summary of Product Characteristics (SPC), as this information is needed mainly by pharmacists.

Related to the third paragraph of page 3/5, the SI system is used for expression of concentration: kg/m^3 or mol/m^3 (or mg/ml and mmol/ml), according to Ph Eur, General Notices, 01/2008:10000. Using percentage as strength for liquid formulations should not be allowed as it represents an additional risk when calculating doses for partial use. For example, in Germany percentage is a common expression for the strength of a solution. Even if EMEA recommends against using percentage, we are worried that if a manufacturer has one solution with strength in percentage already on the market and then decides to register the same solution in another strength through the central procedure, an expression in percent will be allowed. We strongly recommend that the EMEA remove this option.

Three issues are absent from the discussion in the EMEA draft:

1. Expression of strength for fixed dose combinations
2. Expression of strength of active substance versus strength of acid, see footnote 3 on page 3/5.
3. The use of IU as abbreviation for “international units”. IU is easy to confuse with IV or 10. The Institute of Safe Medication Practices has therefore recommended to avoid this abbreviation and use unit.

We strongly urge EMEA to consider these issues either as part of this document or in a follow-up discussion.

Recommendations on the Expression of Strength in the Name of Centrally Authorised Human Medicinal Products

Pharmaceutical form	Single/multi-dose	Preferred strength in the name Amount of active moiety or active substance, as appropriate	Format style
Oral preparation			
Solid unit-dose (e.g. tablets, capsules)	Single dose	Amount per unit dose	x mg
Solid (e.g. granules)	Multi-dose	Amount per unit weight/measuring device	x mg/g/ measuring device
Semi-solid (e.g. oral paste, gel)	Single dose Multi-dose	Amount per unit weight	x mg/g
Liquid preparations (e.g. ampoule ¹ , sachet)	Single dose	Amount per unit volume/weight	x mg/ml/g
Liquid preparations	Single dose Multi-dose	Amount per unit volume/(= y drop(s))	x mg/ml/(= y drop(s))
Powders/granules for liquid preparations	Single dose	Total amount in the container	x mg
Powders/granules for liquid preparations	Multi-dose	Amount per unit volume after reconstitution	x mg/ml
Parenteral preparations			
Liquid preparations	Single dose	Amount per unit volume (+ total amount/total volume) ²	x mg/ml y mg/z ml
Liquid preparations	Multi-dose	Amount per unit volume	x mg/ml
Powders for liquid preparations (without solvent)	Single dose Multi-dose	Total amount in the container	x mg
Powders for liquid preparations (with solvent)	Multi-dose	Total amount in the container (+Amount per unit volume after reconstitution with solvent) ³	x mg x mg/ml
Concentrates	Single dose Multi-dose	Amount per unit volume of the concentrate (before dilution)	x mg/mmol/ml
Implants			
Implants		Total amount in implant	x mg

¹ It is somewhat confusing to use the term ampoule for an oral preparation.

² Added close to the name, written as prominent as expression of strength

³ Added close to the name, written as prominent as expression of strength

Pharmaceutical form	Single/multi-dose	Preferred strength in the name Amount of active moiety or active substance, as appropriate	Format style
Cutaneous, transdermal (according to standard terms), rectal, vaginal, oromucosal and gingival preparations			
Solid preparations (e.g. suppository, tablet, capsule, powder)	Single dose	Amount per unit dose	x mg
Solid preparations (e.g. powder)	Multi-dose	Amount per unit weight	x mg/g
Transdermal preparations (e.g. transdermal patch)	Systemic use	Nominal amount released per unit time (e.g. 24 hours) or total amount in the patch.	x microgram/y hours or
	Local use	Total amount in the patch	x mg
Semi-solid preparations (e.g. cream, gel, ointment)	Multi-dose	Amount per unit weight	x mg/g
Liquids	Single dose	Amount per unit volume	x mg/ml
	Multi-dose		
Preparation for inhalation			
Inhalation products (e.g. hard capsules, pressurised products, gases)	Single or Multi-dose	Amount per delivered dose	x microgram/dose
Nebuliser solution/suspension/emulsion	Single dose	Amount per unit volume	x mg/ml
	Multi-dose		
Eye, ear and nose preparations			
Liquid preparations	Single dose	Amount per unit volume	x mg/ml
	Multi-dose		
Semi-solid preparations (e.g. ointment)	Single dose	Amount per unit weight	x mg/g
	Multi-dose		

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This response arises from the Developing Rational Use of Medicines in Europe project, which has received funding from the European Union, in the framework of the Health programme