European Medicines Agency
Evaluation of Medicines for Human Use

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OVERVIEW OF COMMENTS RECEIVED ON
'COMMUNITY HERBAL MONOGRAPH ON *GENTIANA LUTEA* L., RADIX'
(EMEA/HMPC/578324/2008)

Table 1: Organisations and/or individuals that commented on the draft 'Community herbal monograph on *Gentiana lutea* L., radix' as released for public consultation on 15 April 2009 until 15 July 2009.

	Organisations and/or individuals
1	European Scientific Cooperative on Phytotherapy (ESCOP)
2	Kooperation Phytopharmaka GbR, Germany

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SPECIFIC COMMENTS ON TEXT			
Section number and heading	**Interested party**	**Comment and Rationale**	**Outcome**
2. Qualitative and quantitative composition	ESCOP	The precisely defined herbal preparations b), c) and d) are adequate as examples. However, there is no scientific evidence to justify those specific preparations to the exclusion of any other comparable preparations. More flexibility is needed for traditional use in the absence of controlled studies. **We propose an additional sentence**: Other comparable hydroalcoholic or aqueous extracts.	Not endorsed. The herbal preparations listed are those for which a tradition of 30 years was accepted by the HMPC. For other herbal preparation suitable documentation have not been provided.
4.2. Posology and method of administration	ESCOP	**Posology** Although dyspeptic/gastrointestinal disorders usually are no indication for adolescents above 12, in the indication temporary loss of appetite THMPs from Gentiana lutea L., radix might be used for adolescents as well. **Thus, we propose to delete "and adolescents under 18 years of age" and to use the standard wording "children under 12.**	The use in children and adolescents under 18 years of age is not recommended due to lack of adequate data for a traditional posology. In addition a „loss of appetite by children and adolescents under 18 years of age" should be controlled in any case by a doctor.

5.3.Preclinical safety data	Kooperation Phytopharmaka	We propose to delete the 3rd and 4th paragraph stating "For xanthones ...in those effects:" Rationale: Recent studies do not reveal positive findings for xanthones in general. For this reason the sentences should be deleted. As an alternative, a statement on xanthones (with a specification which xanthones are meant) could be part of the Assessment Report, but not of the text of the monograph. A PubMed database search for "xanthone" and "genotoxic" resulted in two papers: **Tanaka R. Inhibitory effects of xanthone on paraquat- and NaNO(2)-induced genotoxicity in cultures cells. J Toxicol Sci 2007; 32:571-4:** In this contribution, xanthone (as a compound of mangosteens) inhibited the genotoxic effects of paraquat and NaNO(2) in Chinese hamster lung cells at concentrations of more than 5 µM. The results suggest antigenotoxic effects of xanthones. **Rodeiro I, Cancino L, Gonzalez JE et al. Evaluation of the genotoxic potential of Mangifera indica L extract (Vimang), a new natural product with antioxidant activity. Food Chem Toxicol 2006; 44:1707-13:** An extract of the mentioned plant which contains the xanthone mangiferin as main compound was examined in the Ames test (six strains) as well as in the Comet and micronucleus assay. The results suggest that the extract did not induce a mutagenic or genotoxic effect in the used test battery.	Within the AR the positive results of the existing testing are described. Consequently the conclusion was drawn that further testing should be done with *in-vitro* test on mammalian cells according to the "Guideline on the assessment of genotoxicity of herbal medicinal substances/preparations" (EMEA/HMPC/107079/2007). This is reflected within the monograph.