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# EAHP response to the European Commission's consultation on a new Notice on the application of Articles 3, 5 and 7 of Regulation (EC) NO 141/2000 on Orphan Medicinal Products

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The European Association of Hospital Pharmacists (EAHP) welcomes the opportunity to respond to the European Commission's consultation on aspects of the application of Article 3, 5 and 7 of Regulation (EC) N° 141/2000 on orphan medicinal products.

The requirement for a regulation to encourage orphan medicinal product development appears clear and warranted, reflected by mirror regulations in other international markets such as the USA, Australia and Japan. However there is clearly scope for continual improvement in such areas and what follows is a considered opinion from EAHP on how the Commission's current review of Regulation 141/2000 and associated Notices, Communications and Guidance, might provide opportunities for enhancing access and development of orphan medicines.

## Consultation item number 1: Clarification of "significant benefit"

In respect to the proposal to "remove the possibility of claiming a significant benefit based on a potential increased supply", EAHP expresses support for this proposal. As our own research, as well as that of many other organisations, demonstrates, shortage in supply of medicines is a widespread problem across all European countries. Permitting orphan drug designation on the basis of increasing supply, would appear upon first reading to risk providing an unintentional incentive against the manufacturing sector fully addressing the shortage problem. It therefore seems an inappropriate mechanism to combat the problem and a departure from the spirit of the legislation which is to provide incentive for new treatments that represent significant benefit against the pre-existing options.

In respect to the suggestion that "*medicinal products prepared in a (hospital) pharmacy should be considered in the assessment of significant benefit",* EAHP expresses its support for this proposal. To come back to the original intent of the Orphan Drug Regulation, it is to incentivise

the development of new treatments that represent significant benefit against pre-existing options. Hospital pharmacy prepared treatments should certainly be seen as amongst the range of treatments that are considered in this assessment. The inclusion of hospital pharmacy production amongst the range of compared treatments could also be a useful driver to improving information available on this issue.

For similar reasons to those outlined above, EAHP also supports "significant benefit" considerations being extended to comparison against off label use. This again, fits to the spirit of the legislation in respect of incentivizing development of new products that are an advance on treatments already in use. Off label use is a treatment already in use. Once again, the inclusion may also drive improved data collection on this important area of medicines use.

In respect to line 181 of the proposed new Notice, which outlines examples of what 'clinically relevant advantage' could mean, EAHP would like to suggest that clinically relevant advantage be also widely understood as meaning improvements in the ease of administration, safety of the patient, and/or quality of life/options of the patient. This would, as an example, be represented in a switch from intravenous administration to oral administration.

## Consultation item number 2: Encouraging the development of orphan medicinal products for communicable diseases (e.g. Ebola)

EAHP supports the suggested reforms to the regulatory framework designed to encourage orphan drug designation for treatments targeted at low to zero prevalence but infectious diseases in the EU such as Ebola or the Zika virus.

This is fully within the spirit of the legislation in terms of incentivizing the development of treatments for rare conditions that otherwise may not fit within existing market incentives. In this respect we would like to point the Commission to a potentially helpful example where prevailing orphan drug regulation assisted in the development of a vaccine (IXIARO®) for Japanese encephalitis. Suffice to say, major public benefit could be offered by the reform proposed by the Commission.

## Consultation item number 3: parallel authorisation applications

As EAHP understands the matters behind this consultation item, it relates to a highly specific case. It must be seen as regrettable that two sponsors can go through the orphan drug

designation process with little to no knowledge that another company is already working on essentially the same ingredient (e.g Kolbam-Orphaco). To EAHP's mind, the best means to prevent reoccurrence would be to ensure the early dialogue, scientific advice and facilitation processes at the regulatory agency are working efficiently. We do not offer additional comment on this issue other than to suggest that if all is working well in the regulatory framework such occurrences should generally not arise, and therefore the cause of the difficulty may need more attention than the symptom.

## Consultation item number 4: reassessment of orphan criteria for a new subset of the condition

It appears reasonable to EAHP that new therapeutic indications within the same orphan condition be formally verified as being of significant benefit compared to existing treatments and therefore the proposal is supported.

However, on the matter of new indications for orphan drugs, EAHP is conscious of some complaints that the orphan drug designation system could be open to a potential abuse whereby a restricted orphan designation is gained originally with, at later dates, greater and greater number of new indications provided. The Commission might therefore consider whether subsequent reviews of an individual medicine's orphan designation after marketing authorisation should pay attention as to whether the **total** number of patients served by **all** indications of an orphan drug has surpassed to a considerable degree the prevalence of 5 to 10 thousand people in the European Union. In any case, the matter is worthy of attention and reflection by those governing the regulatory framework.

## Consultation item number 5: transfer of orphan designations between sponsors

EAHP supports the reforms proposed by the Commission on the grounds stated in the consultation document: experience suggests existing practice is delaying the placing on the market of generic medicinal product. To our knowledge, there has been only one generic orphan medicine placed on the market with the next to occur in 2018. EAHP would like to point out that there are no biosimilar medicines currently registered as orphan drugs, an issue that should merit Commission attention within its broader review of orphan drug regulation.

## Additional remarks on Orphan Medicines regulation

EAHP notes the section of the consultation preface stating:

> *"This consultation is focused on a number of proposals presented below which reflect the comments and statements made by the Member States and experts at the European Medicines Agency with a view to provide the European Commission with necessary material as a basis for the new notice and, if necessary, for the revision of the Commission Regulation (EC) No 847/2000 of 27 April 2000".*

We wish to take the opportunity of this consultation response to express our recommendation that the Commission's considerations on the orphan drug medicines regulation go wider than simply the proposed new notice, but to the scope for improvements in orphan medicine regulation more widely. 16 years after initial introduction it is an opportune time to commence a broader reflection on the possibilities for improvement and enhancement.

Amongst the short suggestions for consideration within this are:

- The potential case for 'orphan devices' or 'humanitarian use devices', that similarly meets unmet need for very defined patient group for whom commercial incentive for development is otherwise problematic. This could be especially beneficial for instance in respect of paediatric cardiovascular diseases, where devices for adults are otherwise used off-label.
- Mechanisms to meet the difficulties reported of high priced orphan products. For example, there may be scope for greater matching of the regulatory regime to emerging health technology assessment processes and Commission facilitation in joint procurement.
- Improved surveillance and monitoring of the outcomes of treatment by medicines given orphan drug authorization with unsettled benefit-risk profiles at the time of approval e.g. conditional approval. This might be achieved, for example, by improvements to systems of patient registry.
- Potential for improvements to the statutory remit and composition of the EMA orphan medicine committee, and transparency requirements within the original regulation of 2000.