EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL
Health Systems and Products
Medicinal products – authorisations, EMA

<July 13th, 2012>

Submission of comments on PUBLIC CONSULTATION PAPER: Review of the Variations Guidelines (EC) No 1234/2008 Article 4: Review of the Variations Guidelines

Comments from:

Name of organisation or individual
I.P.F.A. International Plasma Fractionation Association

IPFA ref. **IP-12-064**

1. General comments

General comment (if any)
IPFA appreciates and encourage every effort the European Commission undertakes to improve the variations guideline and simplification of the processes and load of work for both regulators and industry. In this context IPFA would like to remind the Commission of the difficulties regarding the PMF second step procedure, as a whole. IPFA (as well as its counterpart PPTA) have already expressed their great concern about the high and unnecessary resource burden for the regulatory authorities and the companies. We also expressed the contradiction with such a procedure with the objective laid down in the European Commission's Better Regulation Initiative. In this present guideline, a pure administrative procedure that does not affect the properties of the final plasma-derived medicinal product requires an immediate notification (IN). IPFA considers this requirement highly unnecessary and this variation would better be classified as a pure notification of the EMA and/or competent authorities.

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*
Page 8	**A5: Change in the name and/or address of a manufacturer of the finished product including importer, batch release or quality control testing sites** Comment: Please clarify the term "*importer*" in this particular subject
Page 12 and page 51	**B.I.a.2.c: The change refers to a biological / immunological substance, or use of a different chemically derived substance in the manufacture of a biological/immunological substance, which may have a significant impact on the quality, safety and efficacy of the medicinal product and is not related to a protocol** **B.II.d.2.c : Substantial change to or replacement of a biological/ immunological/ immunochemical test method or a method using a biological reagent or replacement of a biological reference preparation not covered by an approved protocol** Comment: Does "*protocol*" mean "change management protocol"?
Page 16	**B.I.a.4.page 16 condition 7: The specification parameter does not concern a critical parameter for example any of the following: assay, impurities (unless a particular solvent is definitely not used in the manufacture of the active substance), any critical physical characteristics e.g. particle size, bulk or tapped density, identity test, water, any request for skip testing.** Comment: What is meant by "*assay*"?
Page 73, line 22	**B.V. Changes to a marketing authorisation resulting from other regulatory procedures** **B.V.a) PMF/VAMF** **B.V.a.1 Inclusion of a new, updated or amended Plasma Master File in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure)** **d) Inclusion of an updated/amended Plasma Master File when changes do not affect the properties of the finished product**

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*
	Comment: PMF Second Step Procedures for case d) are categorized as they should be notified as type IA_{IN} procedure type. Proposed change: Such administrative PMF Second Steps Procedures should be notified as type IA procedure type. Rationale: Especially when the MAH is different from the PMF holder, “immediate notifications” of such changes are hardly manageable. Such changes usually impact numerous MAs, MAHs, MSs, type of procedures (MRP/DCP/national/CP), format of dossiers (eCTD, NeeS, paper). They are usually submitted through Worksharing/Grouping procedures which for the initiation cannot be “immediately” managed after receipt of updated certificates from PMF holders. When updated PMF certificates are issued by EMA, a copy of the whole file is immediately dispatched to all MSs, including the list of impacted MAs (Annex A). The MAH considers that when “changes do not affect the properties of the finished product” as for case d), such changes should not require immediate notifications.

Please add more rows if needed.