EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Biologics Working Party (BWP)

Concept paper on the revision of the Guideline on epidemiological data on blood transmissible infections

Agreed by Biologic Working Party	10 April 2024
Adopted by CHMP for release for consultation	15 April 2024
Start of public consultation	30 April 2024
End of consultation (deadline for comments)	28 June 2024

The proposed guideline will replace 'Guideline on epidemiological data on blood transmissible infections' (EMA/CHMP/BWP/548524/2008 rev 1).

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	**Plasma Master File, epidemiology, alert limit calculation, methodology**

1. Introduction

The guideline on epidemiological data on blood transmissible infections (EMA/CHMP/BWP/548524/2008 rev 1) outlines the scientific data requirements for epidemiological data on blood transmissible infections to be included in applications for Plasma Master File (PMF) certification or annual recertification submitted to the EMA.

The guideline requires that a system of alert limits for epidemiological data should be in place to identify individual blood/plasma collection centres with viral infections rates outside the normal range for the given donor population in the PMF (outliers) and to be able to take appropriate corrective actions, if needed. This is an essential part of the measures taken to ensure that donations do not come from donors with a high risk of being infected with blood transmissible agents.

In 2022, as part of a Q&A for PMF holders (PMF-Hs) (EMA/CHMP/BWP/721411/2022) additional guidance encouraged the usage of parametric models for establishing alert limits although clarified that non parametric models might be acceptable, if sufficiently justified.

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In 2023, in view of the experience gathered during the review of the alert limits information in recent PMF annual updates (AU) and the requests from the plasma fractionation industry for further guidance, the need to expand the information for PMF holders on the approach and the statistical method for the appropriate calculation of alert limits was identified.

The revision and expansion on the alert limit calculations of the epidemiological guideline is proposed as part of the 3-year BWP workplan 2024-2026.

2. Problem statement

The current guideline establishes that the criteria in place used by the PMF holder to establish alert limits for epidemiological data, and the system to identify individual blood/plasma collection centres reporting data above the alert limits, should be described.

In order to establish limits that are sufficiently discriminating, the basis for calculation of alert limits for "repeat tested donors" should be kept separate from that for "first time tested donors".

The assessment of the data provided by PMF holders on alert limits since the publication of current guideline has required several rounds of assessment often on several PMF AU procedures for different PMFs, impacting in the PMF certification timelines and resources for all stakeholders. This has prompted the need to revise the Guideline to provide further guidance how alert limits should be established.

3. Discussion (on the problem statement)

Additional guidance on suitable statistical models that could be used in the definition of alert limits was published in an EMA Q&A (EMA/CHMP/BWP/721411/2022). However, experience accumulated in recent years of PMF evaluation reveals that a more detailed guidance for PMF holders needs to be provided on the calculation of alert limits, which impacts on the information to be submitted in the dossier.

This revision will provide guidance in the following aspects:

- Definition of alerts by type of donor (first time tested/repeat tested donors), recovered/source plasma centres and country of origin, geographical area and any other factor;

- Data set on viral marker rates, and time period used for the establishment of the alert limits;

- Criteria for periodic review/recalculation of reference rates and alert limits;

- Cut-off levels for each viral marker that allows the identification of outlying centres;

- Statistical models to calculate reference rates within each PMF as well as alert limits for each individual centre based on the number of donors;

- Data to be submitted by PMF holders on the statistical methodology for the calculation of alert limits necessary for regulatory assessment.

4. Recommendation

The BWP recommends the revision of the Guideline on epidemiological data on blood transmissible infections EMA/CHMP/BWP/548524/2008 Rev. 1 taking into account the issues identified above and aiming to provide further guidance on the calculation of alert limits.

Note: The EMA Q&A (EMA/CHMP/BWP/721411/2022) chapter on Epidemiology may be deleted once the Guideline is updated.

5. Proposed timetable

The revision of the guideline is scheduled to start in 2024 as part of the 3-year BWP workplan. Public consultation is planned for 2 months. It is anticipated that a draft revised guideline will be released for external consultation during 2024.

6. Resource requirements for preparation

The revision of the guideline will be developed by the BWP delegated PMF expert group, and the MWP.

Drafting group meetings (virtual) will be organised, as needed. Monthly teleconferences are foreseen. Preparation of the draft guideline will require discussion at two to three BWP plenary meetings and at one to two MWP meetings.

A PMF alert limits Drafting Group has been set up and is composed of PMF assessors, including one Rapporteur, and MWP members for the revision of the guideline.

7. Impact assessment (anticipated)

It is anticipated that industry and EU regulators will benefit from the proposed revised guideline, which can contribute to the harmonisation of data submission and a better understanding of methods used for the calculation of alert limits. It is expected that the guideline will facilitate the assessment and recertification of the PMF.

8. Interested parties

Interested parties with specific interest in this topic will be consulted during the revision of this guideline, including:

- PMF-holders
- Plasma protein associations (International Plasma and Fractionation Association Comments (IPFA), Plasma Protein Therapeutics Association (PPTA), European Blood Alliance (EBA), etc)
- European Commission (EC), European Directorate for the Quality of Medicines (EDQM) and Europan Centre for Disease Prevention and Control (ECDC)
- Coordination Group for Mutual Recognition and Decentralised Procedures (CMDh)
- Within the European Medicines Agency, there will be consultation with the Biologics Working Party (BWP), Plasma Master File (PMF)-group, Methodology Working Party (MWP), Haematology Working Party (HAEMWP) and Committee for Medicinal Products for Human Use (CHMP).

9. References to literature, guidelines, etc.

Guideline for epidemiological data on blood transmissible infections (EMA/CHMP/BWP/548524/2008 rev 1)

PMF dossier requirements. Questions and Answers for PMF Holders (EMA/CHMP/BWP/721411/2022)

Scientific data requirements for plasma master file - Scientific guideline (EMEA/CHMP/BWP/3794/03)