



## European Federation for Immunogenetics

### Standards for Providers of External Proficiency Testing (EPT) schemes in H&I

These Standards are the minimum criteria required for organizations providing EPT services in H&I (EPT Providers) to conform to the accreditation procedures of EFI. Created and accepted by the EFI EPT Committee in September 2017, modified in January 2018 and approved by the EFI Executive Committee in May 2018. The implementation date for this version 7.2 is July 1st 2018.

#### Change record

Version	Date	Standard	Change reference
7.2	Sep. 17	4.1	EFI Standards Version 7.0 section D1.5 (textual adjustment)
7.2	Sep. 17	4.2	EFI Standards Version 7.0 section D1.5 (textual adjustment)
7.2	Jan. 18	17.1	EPT analysis and assessment according to EFI Standards F1.1 and F2 (textual adjustment)
7.2	Jan. 18	17.2	Standard deleted
7.2	Sep. 17	20	HPA/HNA/KIR/MICA typing scheme assessment (textual adjustments)
7.2	Sep. 17	21	HLA/HPA/HNA/MICA antibody detection scheme assessment (textual adjustments)
7.2	Sep. 17	22	HLA/HPA/HNA/MICA antibody identification scheme assessment (textual adjustments)
7.2	Sep. 17	25	Successful performance in EPT (textual adjustments)
7.1	Nov. 16	4.2	EPT workshops or trials (textual adjustments)
7.1	Nov. 16	7	Number of Participants (new chapter)
7.1	Nov. 16	18	Assessment rules (major textual adjustments)
7.1	Nov. 16	19.4	High or allelic resolution (textual adjustment)
7.1	Nov. 16	25.2	The maximum number of discrepancies allowed (major textual adjustments)

## **1 Staff**

- 1.1 EPT providers must have:
  - 1.1.1 A person with overall responsibility for the scientific direction of the service, e.g. an EPT Director. This function may also be fulfilled by e.g. a Steering/Advisory Committee.
  - 1.1.2 A person with overall responsibility for the day-to-day operation of the service, e.g. an EPT Manager or Technical Supervisor.
- 1.2 The EPT staff must include persons with adequate qualifications and experience in the design, implementation and reporting of EPT schemes or collaborate closely with persons with this expertise.
- 1.3 EPT providers must involve the guidance of persons with detailed technical knowledge and experience of Histocompatibility and Immunogenetics (H&I) test methods and procedures involved.

## **2 Steering/Advisory Committee**

- 2.1 There should be an EPT Steering/Advisory Committee, the names of which are provided in the Prospectus.
- 2.2 This Committee should have at least three members who are external representatives with recognised backgrounds in H&I and/or EPT.
- 2.3 This Committee should meet at least annually to review the conduct and performance of the schemes.
- 2.4 The functions of this advisory Committee must include:
  - 2.4.1 Development and review of procedures for the planning, execution, analysis, reporting and effectiveness of the EPT scheme(s) provided.
  - 2.4.2 Setting performance criteria for EPT schemes.
  - 2.4.3 Providing EPT advice to any accrediting body assessing the technical competence of participating laboratories.
  - 2.4.4 Providing advice to poorly performing participants.
  - 2.4.5 Resolving any disputes between the EPT Director/Manager and participants.
- 2.5 This Committee should also consider written comments from participants, professional organisations and members of the H&I discipline regarding the nature and operation of the schemes provided.

## **3 Annual General Meeting**

- 3.1 There should be an Annual General Meeting at the end of each EPT year; an invitation to attend should be forwarded to each participating laboratory.

## **4 EPT sample numbers per year**

- 4.1 EPT Providers must distribute the minimum number of samples per year for each EPT, as specified in the EFI Standards Version 7.0 section D1.5.

- 4.2 EPT workshops or trials ahead of the establishment of new EPT schemes may use sample numbers less than specified in the EFI Standards Version 7.0 section D1.5.
- 4.3 EPT Providers may use the same samples for more than one EPT scheme. Use of additional samples is optional.

## **5 Test materials**

- 5.1 EPT test materials must resemble routine clinical material as far as possible.
- 5.2 Any conditions relating to the test material which may affect the integrity of the inter-laboratory comparison, such as homogeneity, sampling, stability, possible damage in transit and effects of ambient conditions, should be considered.
- 5.3 Test results must not be disclosed to participants until after the reporting deadline.
- 5.4 Hazards that the test material might pose, must be considered and appropriate action taken to advise any party that might be at risk (test material distributors, participating laboratories) of the potential hazards involved.
- 5.5 Packaging and methods of transport must be adequate to protect the stability and characteristics of the test material.
- 5.6 EPT Providers must comply with National and International regulations applicable to transportation of test materials.

## **6 Scheme registration**

- 6.1 For typing, the loci and typing resolution to be assessed must be documented and laboratories should be allowed to register for combinations of these.
- 6.2 For antibody analysis (detection and /or identification), laboratories should be allowed to register for class I only or class I and class II antibody assessment.
- 6.3 Crossmatching schemes should be designed to reflect current accepted clinical testing practice.

## **7 Number of Participants**

- 7.1 An EPT scheme should include at least ten participants.
- 7.2 If there are less than ten participants the EPT Provider should define the exchange of samples as an EPT workshop or trial.

## **8 Sample distribution**

- 8.1 Any deviations from sample distribution dates must be notified to the participating laboratories.
- 8.2 Samples must be planned to be distributed so that all results can be assessed within the EPT year.

## **9 Prospectus for EPT**

- 9.1 A prospectus or its equivalent e.g. website, must be made available to participating laboratories.

- 9.2 This document must be revised and issued on a yearly basis. It should include the following information:
- 9.2.1 The name and address of the EPT provider.
  - 9.2.2 Contact details for the EPT Director and Manager.
  - 9.2.3 Nature and purpose of the EPT scheme(s) provided.
  - 9.2.4 Requirements for participation in the scheme(s).
  - 9.2.5 The name of the laboratory(ies) responsible for delivering elements of the scheme(s).
  - 9.2.6 Nature of the test materials to be provided.
  - 9.2.7 Description of the manner in which the test items are obtained, processed and transported.
  - 9.2.8 Sample distribution dates and deadlines for reporting.
  - 9.2.9 Description of data/statistical analysis used.
  - 9.2.10 Description of the data or information to be returned to participants.
  - 9.2.11 Description of method(s) used for result evaluation.
  - 9.2.12 The basis of EPT scheme performance evaluation.

## **10 Data processing equipment and analysis**

- 10.1 Equipment used must be adequate to conduct all necessary data entry and statistical analysis to provide timely and valid results.
- 10.2 All software must be validated, supported and backed up.
- 10.3 Storage and security of data files must be controlled.
- 10.4 Statistical models and data analysis techniques should be documented.

## **11 Disagreements**

- 11.1 There must be a documented procedure for instances of formal disagreement (including discrepancies) between the EPT Director/Manager/Steering Committee and a participant laboratory.
- 11.2 There must be an appeals procedure for participants who disagree with their allocated score(s).
- 11.3 Sufficient test material should be retained for the purpose of extended testing.

## **12 Confidentiality and unique laboratory codes**

- 12.1 Unique codes should be assigned to participating laboratories.
- 12.2 Code information should only be known to the participating laboratory and the EPT Provider.
- 12.3 Participants' identity should only be known to the minimum number of people involved in coordinating the EPT programme or providing any remedial advice or action.

### **13 Data analysis**

- 13.1 Participating laboratories' results should be entered and analysed and reported back to the laboratories on or before the deadline stated in the Prospectus.
- 13.2 Data sheets, computer back-up files, printouts, graphs, etc. must be retained for a specified period.

### **14 EPT scheme summary reports**

- 14.1 EPT scheme summary reports must be clear and comprehensive.
- 14.2 EPT scheme summary reports should include data on the distribution of results from all laboratories together with an indication of individual participant's performance.
- 14.3 EPT summary reports should include all data reported by the participants, e.g. low resolution typing schemes should include intermediate level typing results where provided.
- 14.4 The following should be included in EPT scheme summary reports:
  - 14.4.1 Name and address of the EPT Provider.
  - 14.4.2 Date report issued.
  - 14.4.3 EPT scheme and sample information.
  - 14.4.4 Test results listed by laboratory participation code.
  - 14.4.5 Performance information.
  - 14.4.6 Comments on laboratory performance by EPT Director/Manager/technical advisers.
  - 14.4.7 Procedures used to statistically analyse the data.
  - 14.4.8 Details of laboratory methods used should be included for comparison purposes.
- 14.5 Laboratories should not be ranked according to their performance.

### **15 Annual EPT performance certificate**

- 15.1 An annual EPT certificate must be issued to participants summarising their performance.
- 15.2 The annual EPT performance certificate must include:
  - 15.2.1 Name and address of the EPT Provider.
  - 15.2.2 Full name and/or the code of the participant.
  - 15.2.3 Date certificate issued.
  - 15.2.4 Period covered by the EPT.
  - 15.2.5 Name(s) of EPT schemes assessed.
  - 15.2.6 Total number of samples tested.
  - 15.2.7 Participant performance as defined in section 25.
- 15.3 The certificate should be provided on the EPT provider's official paper and be sent to the participants no later than 6 weeks after the end of the EPT year.
- 15.4 Several schemes may be reported on the same document.

15.5 If the annual EPT performance certificate is provided in a language other than English, an English version must be provided for accreditation purposes covering all aspects as stated in section 15.2.

## **16 Communication with participants**

16.1 Participants must be provided with all relevant information on joining an EPT scheme.

16.2 Participants must be immediately advised of any changes in scheme design or operation.

16.3 Feedback from laboratories should be encouraged, so that participants actively contribute to the development of a scheme.

## **17 Nomenclature**

17.1 For EPT analysis and assessment of the results the terminology of HLA and other immunogenetics markers according to EFI Standards F1.1 and F2 must be applied.

## **18 Assessment rules**

18.1 A 75% consensus for all serologically-based EPT should be used. These are serological typing, testing for antibodies (detection and identification) and crossmatching. If a consensus cannot be reached then the results must not be included in the assessment.

18.2 There should be sufficient participants as defined in chapter 7 to allow appropriate analysis to enable a consensus to be assigned in each scheme.

18.3 For all DNA based EPT the EPT Provider may apply a consensus rule to designate the correct result.

18.4 For all DNA based typing EPT there has to be reference typing available to be included in the assessment process of the EPT Provider.

18.5 In an EPT workshop or trial as defined in chapter 7.2 a reference result must be included in the assessment.

18.6 All reference typing must be performed by an EFI or ASHI accredited laboratory.

## **19 HLA typing scheme assessment**

19.1 For HLA typing schemes the entire typing must be correct for a result to be considered correct.

19.2 Serological typing: EPT Providers should ensure that samples distributed for serological HLA typing be DNA typed by the provider or another EFI accredited laboratory before the results are assessed. Providers may adjust their assessment based on this DNA typing. Examples of possible discrepancies:

19.2.1 A participant reports a specificity not included in the consensus type.

19.2.2 A participant fails to report a specificity included in the consensus type.

19.3 Low resolution DNA typing; examples of possible discrepancies:

19.3.1 A participant reports an allele not included in the typing accepted by the Provider.

19.3.2 A participant fails to report an allele included in the typing accepted by the Provider.

19.4 High or allelic resolution DNA typing: HLA alleles must be assessed at high or allelic resolution as defined in the most recent version of the EFI Standards for Histocompatibility Testing. Examples of possible discrepancies:

19.4.1 A participant reports an allele not included in the typing accepted by the Provider.

19.4.2 A participant fails to report an allele included in the typing accepted by the Provider.

## **20 HPA/HNA/KIR/MICA typing scheme assessment**

20.1 HPA/HNA/KIR/MICA typing: Examples of possible discrepancies:

20.1.1 A participant reports an allele/gene not included in the typing accepted by the Provider.

20.1.2 A participant fails to report an allele/gene included in the typing accepted by the Provider.

## **21 HLA/HPA/HNA/MICA antibody detection scheme assessment**

21.1 HLA-class I and class II antibody detection may be assessed separately.

21.2 For HPA/HNA/MICA antibody detection, only results obtained by non-specific assays should be assessed.

21.3 HLA/HPA/HNA/MICA antibody detection: Examples of possible discrepancies:

21.3.1 A participant reports the presence of antibodies where the consensus is negative.

21.3.2 A participant fails to report the presence of antibodies where the consensus is positive.

## **22 HLA/HPA/HNA/MICA antibody identification scheme assessment**

22.1 HLA-class I and class II antibody identification must be assessed separately.

22.2 For HPA/HNA/MICA antibody identification only results obtained by specific assays must be assessed.

22.3 HLA/HPA/HNA/MICA antibody identification: Examples of possible discrepancies:

22.3.1 A participant reports an antibody specificity corresponding to an antigen expressed by the donor of the serum.

22.3.2 A participant reports the presence of an antibody where the consensus is negative.

22.3.3 A participant fails to report an antibody defined to be present by consensus.

22.4 EPT Providers should distinguish between different antibody identification methods if the number of participants allows.

22.4.1 Results from CDC and other assays should be assessed separately.

22.4.2 Results from single antigen assays may be assessed separately.

22.4.3 The 75% consensus should be applied to individual antibody specificities.

22.4.4 An antibody specificity should be assessed as negative if it is reported by 5% or less of the participants.

### **23 Crossmatching scheme assessment**

23.1 Crossmatching scheme assessment: Examples of possible discrepancies:

23.1.1 A participant reports a positive crossmatch where the consensus is negative.

23.1.2 A participant reports a negative crossmatch where the consensus is positive.

### **24 Assessment of haematopoietic chimaerism and engraftment monitoring:**

24.1 The EPT Provider should do a stepwise assessment:

24.1.1 At first a qualitative analysis of the presence of chimaerism should be assessed by consensus.

24.1.2 In a subsequent analysis the percentage of chimaerism should be assessed by an appropriate statistical method.

### **25 Successful performance in EPT**

25.1 Successful performance applies to the annual EPT performance of the laboratory.

25.2 The maximum number of discrepancies allowed is used to determine the acceptable laboratory performance levels:

25.2.1 HPA/HNA/KIR/MICA typing and HLA typing (serological, low, high, allelic resolution DNA-based): 90% correct complete types. A complete type is defined as all loci/genes the laboratory reports for a sample.

25.2.2 HLA/HPA/HNA/MICA antibody detection: 80% correct results of each accredited category.

25.2.3 HLA/HPA/HNA/MICA antibody identification: 75% of the total number of specificities reaching consensus for each accredited category.

25.2.4 Crossmatching: 85% of the total number of results reaching consensus for each accredited category.

25.2.5 Haematopoietic chimaerism and engraftment monitoring EPT must be assessed using established criteria documented as described in sections 9+10.