EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title: Evaluation and certification of quality and non-clinical data relating to advanced therapy medicinal products		
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1. Purpose

This SOP describes the procedure for the evaluation and certification of quality and, where applicable, non-clinical data submitted by micro, small and medium-sized enterprises developing advanced therapy medicinal products.

2. Scope

This SOP applies to the Biologicals Section, the Scientific Support and Projects Section, the Safety and Efficacy of Medicines Sector in the Human Medicines Development and Evaluation Unit, the Regulatory Affairs Section, the Scientific Committee Support Section (CAT Secretariat), the Compliance and Inspection Sector in the Patient Health Protection Unit, the Product and Application Business Support Section in the Veterinary Medicines and Product Data Management Unit, and the Legal Service Sector in Directorate.

3. Responsibilities

It is the responsibility of each Head of Sector/Section to ensure that this procedure is adhered to within his/her own sector/section. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9.

4. Changes since last revision

New SOP.

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5. Documents needed for this SOP

- Template 1 - Application form (located in SIAMED II)
- Template 2 – Eligibility (located in SIAMED II)
- Template 3 - Validation form checklist (located in SIAMED II)
- Template 4 – validation letter (located in SIAMED II)
- Template 5 – Certification evaluation report (located in SIAMED II)
- Template 6 – Peer review template (located in SIAMED II)
- Template 7 – BWP report template (located in SIAMED II)
- Template 8 - Opinion templates (located in SIAMED II)
- Template 9 - Certificate template and advisory letter (located in SIAMED II)

6. Related documents

EMEA/CAT/418458/2008: Procedural advice on the certification of quality and non clinical data for small and medium sized enterprises developing advanced therapy medicinal products (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000300.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058007f4bd)

EMEA/CAT/486831/2008: Scientific guideline on the minimum quality and non clinical data for certification of advanced therapy medicinal products (http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000300.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058007f4bd)

EMA/354785/2010: Procedural advice on the evaluation of combined advanced therapy medicinal products and the consultation of Notified Bodies in accordance with Article 9 of Regulation (EC) No. 1394/2007 (http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2011/03/WC500102598.pdf)

SOP/EMA/0101: Conducting checks for conflicts of interest when assigning medicinal products for human or veterinary use to Agency employees

SOP/INSP/2001: Coordination of site visits in the context of the certification of quality and non-clinical data submitted by SMEs developing ATMPs

WIN/H/3111: Pre-submission meetings

SOP/H/3309: Procedure for provision of scientific recommendation on classification of ATMPs

7. Definitions

ATMP: Advanced therapy medicinal product

CAT: Committee for Advanced Therapies

CAT coordinator: CAT member acting as rapporteur for the certification procedure

D-LS: Legal Service Sector

EMA: European Medicines Agency

HoS: Head of Sector

PTL: Product team leader (scientific administrator from H-QM-BIO responsible for the procedure. Also referred to as EMA coordinator in EMEA/CAT/418458/2008.)

H-HM-SSP: Scientific Support and Projects Section

H-QM-BIO: Biologicals Section

H-SE: Safety and Efficacy of Medicines Sector

PTM: Product team member appointed from one of the following sectors/sections (H-SE, H-HM-SSP, P-CI-CNC, P-CI-MQC, P-R-RA and D-LS)

Resource coordinator: Assistant in H-QM-BIO responsible for data entry in SIAMED II

RSI: Request for supplementary information

SH: Section Head

SME: Micro, small and medium-sized enterprise

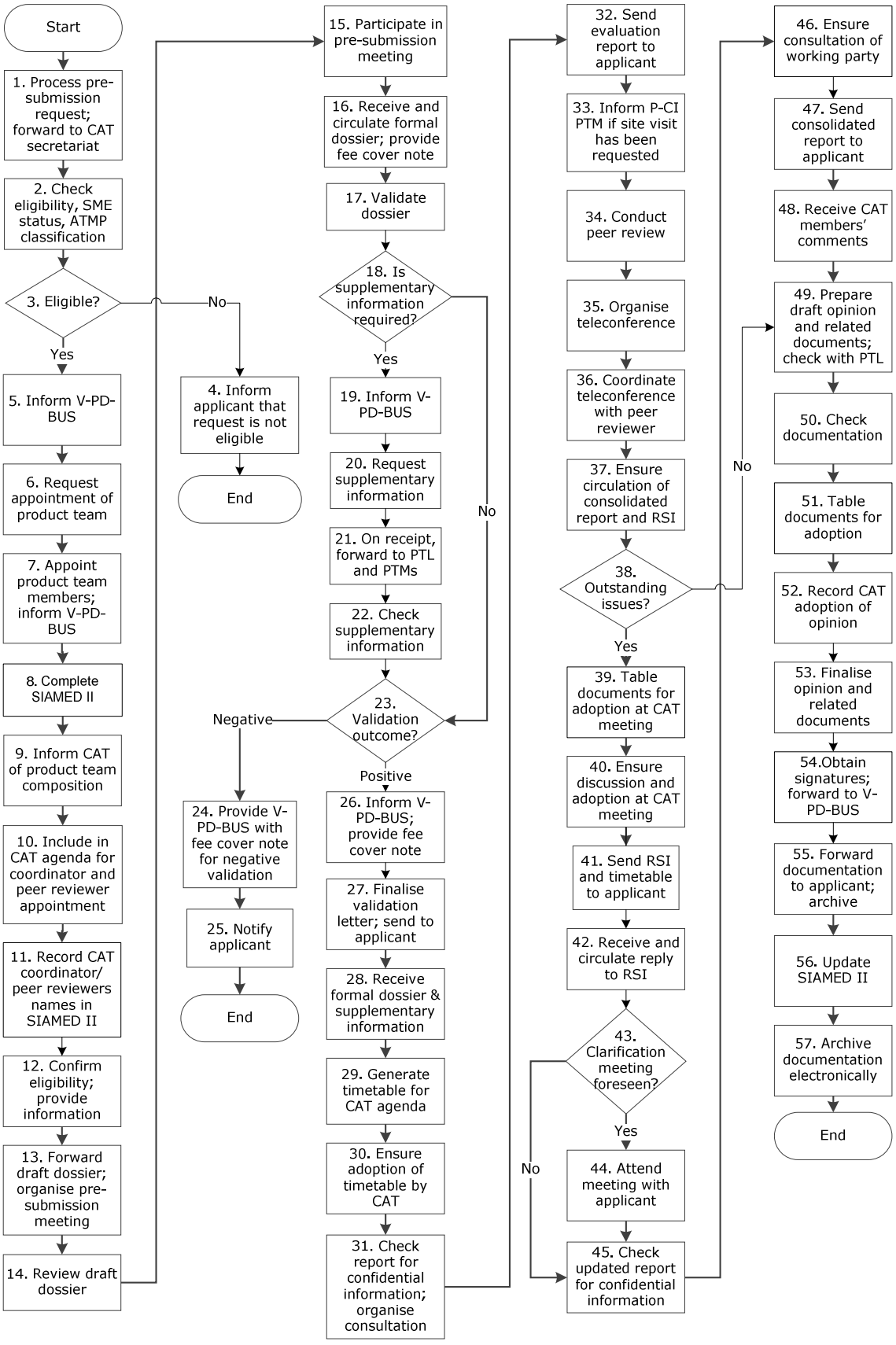
P-CI-CNC: Clinical and Non-clinical Compliance Section

P-CI-MQC: Manufacturing and Quality Compliance Section

P-R-RA: Regulatory Affairs Section

V-PD-BUS: Product and Application Business Support Section

8. Process map(s)/ flow chart(s)



9. Procedure

Step	Action	Responsibility
	Eligibility	
1	Day -70: Receive pre-submission request form (intent to submit ATMP certification - template 1 (application form)) and draft certification dossier. Enter the information in SIAMED II. Forward the pre-submission request form to CAT secretariat.	V-PD-BUS
2	Check the eligibility for the certification procedure: • SME status (check with SME Office) • ATMP classification (refer to SOP/H/3309 if there is need for ATMP classification).	CAT secretariat
3	If request is not eligible, go to step 4. If request is eligible, go to step 5.	CAT secretariat
4	Inform the applicant by letter (template 2) that the request is not eligible. End of procedure.	CAT secretariat
5	Inform V-PD-BUS that the request for certification is eligible and inform if a pre-submission meeting has been requested by the applicant.	CAT secretariat's assistant
6	Request appointment of product team (PTL in H-QM-BIO and PTMs in H-SE, P-R-RA, D-LS, H-HM-SSP, P-CI-MQC and P-CI-CNC, as applicable).	V-PD-BUS,
7	Appoint respective PTL and PTMs and inform resource coordinator. Conduct checks for conflicts of interest, where required (refer to SOP/EMA/0101). Inform V-PD-BUS.	SH (H-QM-BIO, H-SE, P-R-RA, H-HM-SSP, P-CI-MQC, P-CI-CNC, D-LS)
8	Record pre-submission request form and composition of product team in SIAMED II.	Resource coordinator
9	Inform the CAT secretariat of the composition of the product team.	V-PD-BUS
10	Day -60: Include the request for certification in the agenda of the CAT meeting and table the request form in MMD for the next CAT meeting for discussion. *Note: The CAT appoints CAT members as CAT coordinator and as*	CAT secretariat

Step	Action	Responsibility
	CAT peer reviewers for this procedure.	
11	Record names of CAT coordinator and peer reviewers in SIAMED II. Inform V-PD-BUS and the PTL of the names.	CAT secretariat's assistant
12	Inform the applicant by letter that the product is eligible for the certification procedure, provide the names of the PTL, CAT coordinator and CAT peer reviewers, and provide the timetable for submission.	V-PD-BUS
	Pre-submission	
13	Day -50: Provide the PTL and PTMs with the draft dossier received from the applicant. Organise a pre-submission meeting (teleconference) with the PTL, relevant PTMs, CAT coordinator and CAT peer reviewers, if required (refer to WIN/H/3111). *Note: The draft dossier is sent by the applicant directly to the CAT coordinator and CAT peer reviewers.*	V-PD-BUS
14	Review draft dossier in advance of the pre-submission meeting. *Note: The CAT coordinator and CAT peer reviewers also review the draft dossier in advance of the pre-submission meeting.*	PTL and relevant PTMs
15	Days -40 to -20: Participate in the pre-submission meeting (teleconference), if applicable. Review pre-submission meeting minutes provided by the applicant. *Note: CAT coordinator and CAT peer reviewers will also participate in the teleconference.*	PTL and relevant PTMs,
	Validation	
16	Day -10: Receive formal certification dossier from the applicant. Provide the PTL and PTMs with the certification dossier for validation. Provide fee cover note to PTL.	V-PD-BUS
17	Perform validation and consult with relevant PTMs when applicable. Complete the validation checklist (as indicated in template 3).	PTL and relevant PTMs
18	If supplementary information is required from the applicant, go to step 19. If no supplementary information is required, go to step 23.	PTL

Step	Action	Responsibility
19	Inform V-PD-BUS of the supplementary information that is required from the applicant.	PTL
20	Request supplementary information by Eudralink from the applicant and confirm the deadline.	V-PD-BUS
21	On receipt of supplementary information inform PTL and provide it to the relevant PTMs.	V-PD-BUS
22	Check the supplementary information received and continue with the validation.	PTL and relevant PTMs
23	If the outcome of validation is negative, go to step 24. If the outcome of validation is positive, go to step 26.	PTL
24	Provide V-PD-BUS with the fee cover note for a negative validation indicating the SME status for a fee waiver.	PTL
25	Inform applicant of negative validation. End of procedure.	V-PD-BUS
26	Inform V-PD-BUS that the outcome of validation is positive and provide the completed fee cover note (consult RA PTM if necessary).	PTL
27	Generate validation letter and request the PTL to sign it. Send signed validation letter to applicant (template 4).	V-PD-BUS
28	Day -5: Receive formal certification dossier (including supplementary information) from applicant. *Note: The CAT coordinator, CAT peer reviewers and CAT members will also receive the formal certification dossier.*	V-PD-BUS
29	Generate timetable and forward it to CAT secretariat for inclusion in the CAT meeting agenda.	V-PD-BUS
30	Day 0: Start of procedure Include the request for certification in the agenda of the CAT meeting and table the timetable in MMD for the next CAT meeting for adoption. Record the adoption of the timetable in the minutes and table of decision of the meeting.	CAT secretariat
	Evaluation	
31	Day 40: Ensure that the CAT coordinator circulates the evaluation report (template 5). Forward the evaluation report to the relevant PTMs and PTL's	PTL

Step	Action	Responsibility
	assistant. Check the evaluation report and delete any (confidential) information, if applicable. Inform PTL's assistant. *Note: the CAT coordinator performs the evaluation and circulates the evaluation report to CAT members and PTL (if applicable identify need for consultation of relevant expert groups, working parties or notified body or site visit).* If applicable, organise consultation of relevant working party or notified body (refer to the procedural advice on consultation of notified bodies for combined ATMP). Forward outcome of working party consultation to CAT coordinator for inclusion in consolidated evaluation report.	
32	Send redacted evaluation report by Eudralink to the applicant.	PTL's assistant
33	Inform the P-CI PTM if a site visit has been requested (refer to SOP/INSP/2001).	PTL
34.	Conduct peer review	PTL and relevant PTMs
35	Days 50 - 55: Organise teleconference with PTL, CAT coordinator and CAT peer reviewers.	PTL's assistant
36	Coordinate the peer review teleconference. *Note: the CAT peer reviewers and CAT members conduct the peer review and prepare comments on the evaluation report (see template 6) for the peer review teleconference*	PTL
37	Day 55: Ensure that the CAT coordinator circulates the consolidated evaluation report and RSI, if applicable, to PTL and CAT members.	PTL
38	If there are outstanding issues, go to step 39. If there are no outstanding issues, go to step 49.	PTL
39	Day 60: Table the consolidated evaluation report, draft RSI, draft site visit request and/or draft request for consultation of a notified body in MMD for discussion and adoption at the next CAT meeting.	PTL's assistant
40	If applicable, during CAT meeting ensure: • Discussion and adoption of site visit request (see SOP/INSP/2001) • Discussion and adoption of consultation of a notified body • Discussion and adoption of RSI. Inform the PTL's assistant of the	CAT secretariat

Step	Action	Responsibility
	RSI. *Note: The clock is stopped if any of the above is agreed.*	
41	Day 60: If applicable, send adopted RSI and response timetable by Eudralink to applicant. *Note: Clock stop should be for 1 month and can be extended to 2 months, except for notified body consultation and site visit where the procedure restarts as soon as the site visit report or the results of the assessment by a notified body are made available.*	V-PD-BUS
42	Day 61: Receive written explanation to RSI from applicant. Forward to PTL and product team. *Note: The response to RSI is sent by the applicant directly to the CAT coordinator and CAT peer reviewers.*	V-PD-BUS
43	If clarification meeting has been foreseen, go to step 44. If no clarification meeting is foreseen, clock re-starts. Go to step 45.	PTL and relevant PTMs
44	Clock re-start: Attend clarification meeting with applicant. *Note: The clarification meeting takes place at the CAT plenary meeting.*	PTL and relevant PTMs
45	Days 62 - 75: Ensure that the CAT coordinator evaluates responses and sends the updated and consolidated evaluation report to the CAT members and the PTL for comments. Check the consolidated evaluation report and delete any (confidential) information, if applicable. Inform PTL's assistant.	PTL
46	Ensure that consultation of relevant working party (e.g. BWP see template 7) takes place.	PTL
47	Send consolidated evaluation report by Eudralink to the applicant.	PTL's assistant
48	Receive comments on the consolidated evaluation report of the CAT coordinator from CAT members.	PTL
49	Day 55 (from step 38) or Day 85 (from step 48): Prepare opinion, draft certificate or advisory letter, and evaluation report (see template 8 and 9). Prepare transmission slip. Check documents with the PTL and circulate with transmission slip to the product team.	PTL's assistant

Step	Action	Responsibility
50	Check draft opinion, certificate or advisory letter, and evaluation report.	PTM (P-R-RA, D-LS, H-SE (if applicable)) followed by HoS H-QM (back up: SH H-QM-BIO)
51	Day 60 or Day 90: Table the draft opinion, certificate or advisory letter and evaluation report in MMD for discussion and adoption.	PTL's assistant
52	Record the adoption in the minutes and table of decisions of the meetings	CAT Secretariat
53	Finalise opinion, draft certificate or advisory letter, and evaluation report taking into account the discussion at the CAT meeting, if applicable.	PTL
54	Obtain signatures of HoS H-QM and CAT chair. Forward all documents to V-PD-BUS.	PTL's assistant
55	Send signed certificate or advisory letter, signed opinion and certification evaluation report to applicant. Archive documentation.	V-PD-BUS
56	Update SIAMED II with the outcome of the certification procedure.	CAT secretariat's assistant
57	Archive electronically the documents in DREAM	PTL's assistant

10. Records

All required documents received and/or generated during this procedure are saved electronically in the product folder in DREAM:

01. Evaluation of medicines\H-AT\Certification\<PRODUCT NAME><PROCEDURE NUMBER>

The following documents are considered as a record (retention time: 30 years):

- Cover letter with date-in stamp (scan of document)
- Certification dossier from applicant
- Supplementary information submitted by the applicant
- Validation letter (scan of signed document)
- Consolidated evaluation report
- Adopted RSI
- Responses to request for supplementary information from applicant
- Site visit report

- Advice from notified body
- Final consolidated evaluation report
- Opinion, certificate or advisory letter, evaluation report (scan of signed document)