European Medicines Agency
Work Instructions

Title: Validation of Scientific Advice and Protocol Assistance Requests		
Applies to: Scientific Advice and Orphan Drugs Sector (Scientific Advice Section)		
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1. Changes since last revision

The former SOP has been reformatted as a WIN and has been revised in line with changes to the scientific advice procedure and the method of fee payments.

2. Records

Records are kept in the master file. Electronic records are saved in the appropriate folders in EDMS.

3. Documents needed for this WIN

- Template 1: Form for cover sheet merge (located at X:\Templates\Others\H – Scientific advice)
- Annex 1: Requirements for structure and content of scientific advice/protocol assistance draft request

4. Related documents

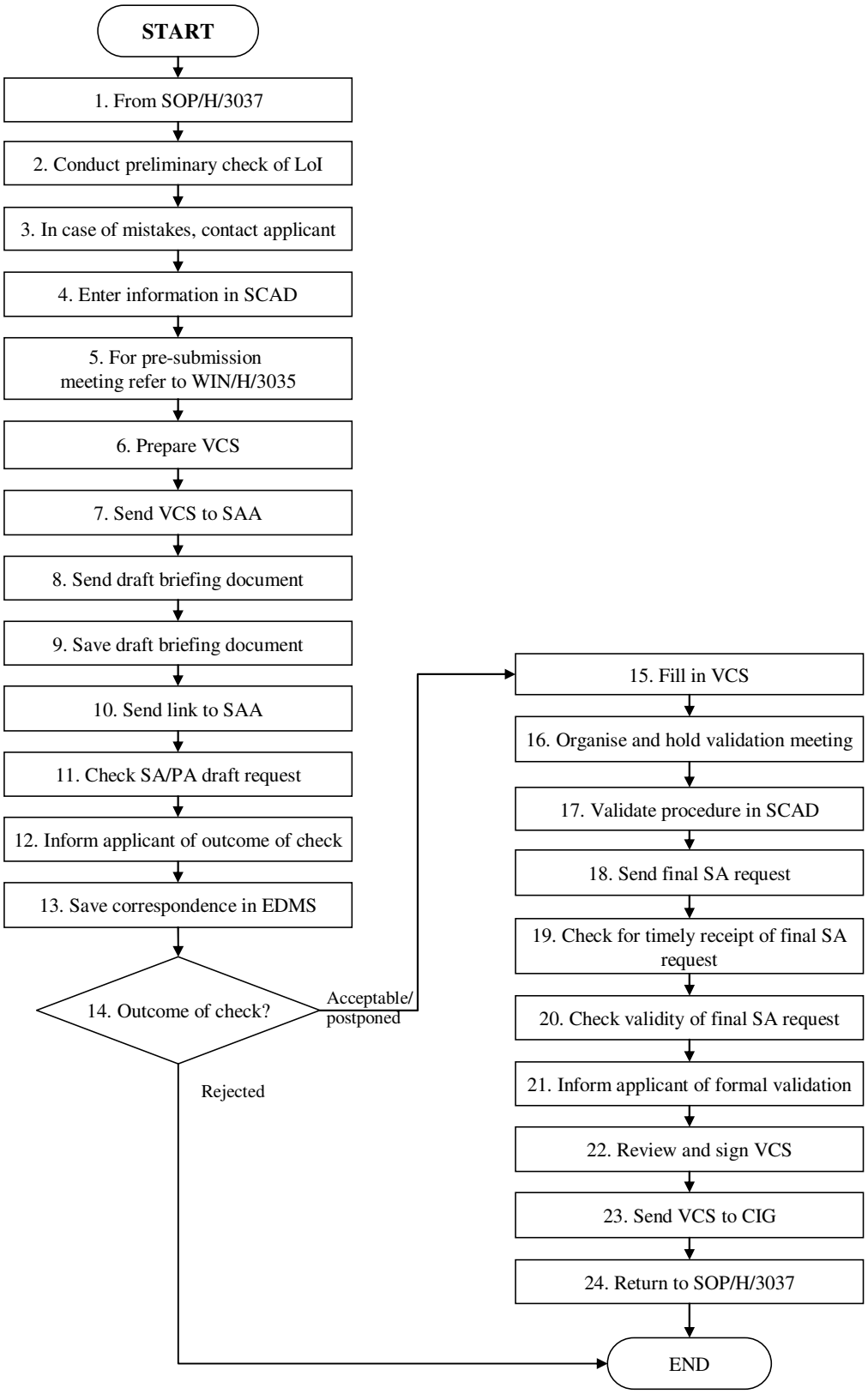
- Email text for validation and start of procedure e-mail (documentum\Docbases\EDMS\Meetings\Scientific Meetings\SAWP\SA Secretaries Working Folders\Secretaries templates\New requests and presub meetings\(N) 2 - Validation and start of procedure email)
- Rules for the implementation of Regulation (EC) N. 297/95 as amended on fees payable to the European Medicines Agency and other measures (http://www.emea.europa.eu/htms/general/admin/fees/implementing_rules.pdf)
- Explanatory Note On Fees Payable To The EMEA (http://www.emea.europa.eu/htms/human/presub/13575708en.pdf)
- Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use, as amended
- SOP/EMEA/0038 on SME fee reductions, fee deferrals and conditional fee exemptions
- WIN/H/3035 on Organisation of scientific advice and protocol assistance pre-submission meetings
- WIN/H/3036: General dealings between SAWP Secretariat and working parties, SAGs, committees and patients' organisations
- SOP/H/3037 on Scientific Advice and Protocol Assistance Procedure
- WIN/H/3040 on Use of scientific advice and protocol assistance database
- SOP/H/3048 on Processing of fee reductions for designated orphan medicinal products
- SOP/H/3101 on Determination of fees (Medicinal products for human use)
- Dates of SAWP meetings and deadlines for scientific advice or protocol assistance request submissions (http://www.emea.europa.eu/htms/human/sciadvice/Scientific.htm)

5. Definitions

AA: Administrative Assistant
ATMP: Advanced therapy medicinal product
BMWP: ad hoc Similar Biological (Biosimilar) Medicinal Products Working Party
BPWP: Blood Products Working Party
BWP: Biologics Working Party
CIG: Central Information Group
CPWP: Cell-based Products Working Party
FU: Follow-up request; a follow up to initial request is defined as any subsequent request falling within the same therapeutic indication and initial area(s) as the initial request (area means main area of advice: Quality – Clinical – Preclinical).
GTWP: Gene Therapy Working Party
LoI: Letter of Intent
OMP: designated orphan medicinal product
PA: protocol assistance
PgWP: Pharmacogenomics Working Party
QWP: Quality Working Party
RAOS: Regulatory Affairs and Organisational Support Sector
SA: scientific advice
SAA: Scientific Advice Administrator
SAA(SAWP): Scientific Advice Administrator responsible for SAWP secretariat
SAWP: Scientific Advice Working Party
SCAD: Scientific Advice database
Sec: Secretary
SME: Small and Medium-sized Enterprises
SWP: Safety Working Party
VCS: Validation cover sheet
VWP: Vaccine Working Party

 : Symbol denoting critical step

6. Flow Chart


START
1. From SOP/H/3037
2. Conduct preliminary check of LoI
3. In case of mistakes, contact applicant
4. Enter information in SCAD
5. For pre-submission meeting refer to WIN/H/3035
6. Prepare VCS
7. Send VCS to SAA
8. Send draft briefing document
9. Save draft briefing document
10. Send link to SAA
11. Check SA/PA draft request
12. Inform applicant of outcome of check
13. Save correspondence in EDMS
14. Outcome of check?
Acceptable/ postponed
Rejected
15. Fill in VCS
16. Organise and hold validation meeting
17. Validate procedure in SCAD
18. Send final SA request
19. Check for timely receipt of final SA request
20. Check validity of final SA request
21. Inform applicant of formal validation
22. Review and sign VCS
23. Send VCS to CIG
24. Return to SOP/H/3037
END

7. Instructions

Step	Action	Responsibility
Just after the deadline for submission of Letter of Intent		
1	From SOP/H/3037	
2	Conduct a preliminary check of the LoI to be able to categorize the procedure for the following: • Follow-up request or subsequent request (search and compare in the scientific advice database) • Protocol Assistance or Scientific Advice • Special requests (broader advice, conditional authorisation etc.) • SME status • Indication • Area of advice (quality, preclinical, clinical and significant benefit) • Paediatric involvement • Splitting of request (e.g. two indications or FU vs new request)	AA/SAA(SAWP)
3	If mistakes are found in the LoI, contact the applicant and ask them to resubmit an updated version of the LoI.	Sec
Before creating the agenda		
4	Enter the information from the LoI into the SCAD (refer to WIN/H/3040).	AA/Sec
5	If a presubmission meeting has been requested refer to WIN/H/3035.	Sec
6	Prepare VCS containing background information on the new request (by merging LoI form to template 1).	AA
7	Link VCS to product folder in EDMS and send locator to the responsible SAA with deadlines.	AA
8	Send draft briefing document (or updated in case of presubmission meeting) to the scientific advice inbox.	Applicant
9	Save draft briefing documents to product folder in EDMS.	Sec
10	Send the link to the saved products to the responsible SAA.	Sec
At least a week before the deadline for final submission (products without presubmission meeting: day -30 to -10, products with presubmission meeting: from the presubmission meeting day to day -5).		
11	Check scientific advice/protocol assistance draft request with respect to its structure and content (refer to Annex 1 for requirements).	SAA
12	Review the request and decide whether request is acceptable or not (with e.g. support from Quality of Medicines Sector or from Paediatric section, as necessary). • Request is acceptable (with or without comments). • Request is to be postponed due to unacceptable content and company does not have time to incorporate comments for the start of procedure. • Request is out of the scope of SA or PA therefore rejected. Communicate the decision to the applicant via email. If preferred, comments can be discussed with the company over the phone but the validation comments should be sent to the applicant in writing. (See template text in Section 7) Copy the responsible secretary in the correspondence. Where applicable advise applicant to submit any regulatory and legal questions to RAOS via e-mail.	SAA
13	Save email correspondence to EDMS product folder.	Sec

Step	Action	Responsibility
14	Depending on the outcome of step 11: If the request is acceptable, go to step 15. If the request is postponed, go to step 15 after the applicable time delay. If the request is rejected, procedure ends.	SAA
Day -15 to -5		
15	 Fill in VCS by checking applicant's data (and correct if necessary): • assign correct fee level and fee (see SOP/H/3101) • tick relevant boxes for the product development • check for SME, ATMP and PA fee waivers/reduction and ad hoc fee reduction (e.g. pandemic influenza vaccines). • tick relevant box if paediatric only or mixed paediatric request. • tick Working Parties involvement (see also WIN/H/3036) o VWP: if viral vaccine (not cancer vaccine), quality, preclinical and clinical questions. o BWP: if biological product quality questions. o QWP: if chemical product quality questions. o BMWP: if biosimilar products preclinical and clinical questions. o SWP: for all preclinical questions. o BPWP: if blood products clinical questions. o GTWP: if gene therapy products clinical questions. o CPWP: if cell based products clinical questions. o PgWP: only if very specific questions on pharmacogenetics.	SAA
16	Organise and attend validation meeting in order to brief and discuss procedures and review the status.	SAAs/AA/Team leader
17	Complete VCS by validating procedures in SCAD: • insert date of submission and validation in Procedure Workflow • insert the automatically assigned procedure number in the LoI • check if correct fee waiver requests (SME or PA) have been received and logged by the relevant EMEA offices (SME Office or orphans team). If not, request the company to act. If not eligible for fee waivers, inform immediately the company of non-eligibility and the amount of fee they will receive. • Check if initial area advice in database corresponds to validated VCS • Check if fee level of database matches the VCS	AA/Sec
In line with published deadlines		
18	Send Final Scientific Advice request (1 CD and 1 paper version) within the published deadline to SAWP Secretariat (Scientific Advice inbox).	Applicant
19	Check that Final Scientific Advice request is received within the published deadline. Note: It is the applicant's responsibility to make sure that the request arrived at its destination.	Sec
20	Check the Final Scientific Advice request is valid and contains all relevant information (either the final electronic version or the paper version). If the request is not complete contact the applicant and request the missing information.	SAA
21	Announce formal validation of request to the applicant by email.	Sec

Step	Action	Responsibility
Around day 0		
22 	Review and Sign VCS	SAA
23	Send original and signed VCS that doubles as a fee cover note (according to SOP/H/3101) to AA at CIG. If available separately, send to CIG also information on purchase order or number for invoicing purposes.	AA/Sec
24	Return to SOP/H/3037.	

8. Example text for validation comments

Dear <<name>>,

I have read through your briefing document for Scientific Advice/Protocol Assistance for <<product>> and I have the following comments that would improve the package:

- <<comments>>

Please do not hesitate to contact me if you have any further questions.
Kind regards
<<SAA name and contact details>>

Annex 1

Requirements for structure and content of scientific advice/protocol assistance draft request

The request should be presented as follows:

1. Letter of Intent
2. Table of contents of the request
3. Briefing document including the questions and applicant's position

The briefing document is the most important section of the request. This review of the request for scientific advice or protocol assistance by the SAWP will primarily be based on the questions and applicant's positions presented by the applicant in the briefing document. The following should also be provided in an introductory section:

- background information about the product,
- background information on the disease to be treated,
- the intended indications planned to be supported by the development programme,
- the worldwide regulatory status of the product,
- for OMP, list of OMP with a centralised MA for the same indication
- the stage of development (pharmaceutical, preclinical, clinical) and in particular the stage(s) of clinical study(ies) proposed (completed, ongoing, planned). For ongoing clinical studies the percentage of recruitment achieved at time of submission of the request for scientific advice or protocol assistance should be highlighted.
- where applicable, a short overview table listing data requirements described in Annex I to Directive 2001/83/EC for development programmes which intend to use published scientific literature to support a future MAA application ("mixed data", bibliographical and abridged applications) outlining
  a) presence ***or*** absence of data for each requirement including justification where data are not to be provided.
  b) nature of data (original results of tests and trials/own data ***or*** published scientific literature)
  c) use of published scientific literature (as supportive ***or*** in order to replace any tests or trials).

The questions are *ordered* and *numbered sequentially* to address scientific issues (order: quality/pre-clinical/clinical issues/significant benefit). Multidisciplinary questions should be labelled accordingly.

Each question is followed by a ***separate*** company's position including a justification(s) of the company strategy for each topic, together with cross-references to the relevant parts of the annexes as needed. The company's position should be summarised after each question in the briefing document.

4. Appendices

The appendices may include e.g.

- Background information (product profile if available, investigators' brochure)
- Information relating to the questions (e.g. relevant study protocols – as detailed as possible or draft study protocol or study outlines, questionnaires, scales etc.)
- Bibliographical data (full text references)
- Content of previous scientific advice received (national EU Authorities, other relevant International authorities, eg FDA)
- Relevant guidelines (other than CHMP guidance documents)
- Contract agreement when the request is submitted by a consultant/CRO on behalf of the company