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Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

DSEB

Operations	Drug Safety and Evaluation Branch
Procedure	DSEB SOP – 0928 **ADMINISTRATION OF THE PHARMACEUTICAL CHEMISTRY EVALUATION SECTION EXTERNAL EVALUATION PROGRAM**
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1. AIM/PURPOSE/SCOPE

This SOP details the procedures for using external evaluators to evaluate data otherwise evaluated by the Pharmaceutical Chemistry Evaluation Section (PCES).

2. RESPONSIBILITY

This SOP covers the activity of PCES of the Drug Safety and Evaluation Branch (DSEB).

Responsibility for the revision and maintenance of this document rests with the Section Head, in consultation with the relevant evaluation and administrative staff within and outside the Section.

3. INTRODUCTION/BACKGROUND

Where appropriate, and with the Section Head's consent, the PCES contracts external evaluators to carry out the evaluation of some of the chemical, pharmaceutical and biopharmaceutical data submitted in support of Category 1 and 3 applications.

Within the PCES, a senior evaluator, the External Evaluation Coordinator (EEC) coordinates the external evaluation program.

The senior evaluator within the stream responsible for the application selects the papers to be sent to the external evaluator, and assesses and processes the external evaluation report(s) once received from the external evaluator.

The Clinical Executive Assistants (EAs) are responsible for the administrative and other clerical procedures.

4. PROCEDURE/POLICY

The steps involved in the procedure for external evaluations are as follows:

1. The senior evaluator responsible for the product obtains the Section Head's approval for the external evaluation of data.

2. The senior evaluator requests the EEC to arrange an external evaluator to carry out the evaluation.

3. The senior evaluator gives the EEC the relevant chem/biol file, a completed (pink) PCE Data Allocation Sheet and the data (plus any miscellaneous attachments) that need to go to the external evaluator.

   Where an application contains more than one biopharmaceutic study, guidance should be given to the external evaluator about which studies should be evaluated in full, which should be summarised only, and which should be ignored. The relevant stream senior evaluator should do this and fill in a "Note to External Evaluators of Biopharmaceutic Data" (Proforma P6). Include this proforma amongst the materials to be sent to the evaluator. Make an extra copy for the relevant chem/biol file.

   The nature of the assay method used and of each relevant study should be checked since this has implications for fee calculations. The fee takes into account the number of studies to be evaluated and whether more than one assay method is involved. The number of treatments involved in each study and the number of analytes assayed (eg. unchanged drug, active metabolites and/or the second drug in a fixed combination preparation) should be stated.

   If not already in the volume of chemistry, pharmaceutical and biopharmaceutical data, include copies of the following:

   - relevant company letters of application;
   - any explanatory notes deemed necessary and/or relevant file material (including old evaluation reports, filter reports and a summary of biopharmaceutic studies if appropriate).

4. The EEC arranges with a suitable external evaluator to carry out the evaluation, enters an External Evaluation event in PREMIER and prepares:
   a. a Minute (with a copy of the PREMIER External Evaluation record) for the Section Head's signature and the Branch Director's approval, and
   b. a PCE Instruction Sheet which he emails to the Executive Assistants (EAs).

5. The PCE Section Head signs the Minute (with attachments) and forwards it and the EAs.

6. The EAs make a copy of the Minute and hold this and send the original to the Branch Director for signature.

7. The Branch Director signs the Minute and forwards it to the DSEB Finance Officer.

8. The Finance Officer keeps the signed original Minute and forwards a copy to the EAs.

9. The EAs prepare the required contract documents in accordance with Branch Instructions.

   The usual contract time is **2 months** from the date of receipt of data for a major evaluation (biopharmaceutical data and/or chemical and pharmaceutical data). For review of replies to questions the time is **4 weeks**. Times can be adjusted according to the amount of work to be done, the urgency with which it is required and, if necessary, whether a bonus is to be paid. Timeframes other than the nominal ones should be agreed with the evaluator in advance. The fee for each contract is calculated taking into account the Schedule of target times for external evaluators in the attached Appendix.

10. The EAs send a covering letter and the 2 unsigned contact documents (one white copy and one yellow copy) to the external evaluator for signature. **No changes can be made to the contract by any area.**

11. The external evaluator signs the contract documents and returns both copies to the EAs.

12. The EAs prepare a Contract Purchase Order and forward this and the contract documents to the PCE Section Head (if the contract amount is $20,000 or less) or to the Head of the Management Coordination Unit (if the contract amount is more than $20,000) for signature.

13. The relevant Section Head (PCE or Management Coordination) signs the Purchase Order and both copies of the contract on behalf of TGA (a witness also signs the contract documents) and returns the signed documents to the EAs for processing.

14. The EAs send 1 copy (white) of the signed contract to the external evaluator and put the other copy (coloured) on the relevant coordination file

15. The EAs forward a file note indicating that the contract has been signed, a copy of the PCE Instruction Sheet and a copy of the Schedule from the contract to the EEC to be placed on the relevant chem/biol file.

16. The EAs (or the EEC) send a request to TGA Records Management Section (RMS) to collect, package and dispatch the relevant data to the external evaluator.

17. The RMS collects the data from the PCE Section, packs and dispatches the data together with the attachments and a return Courier Voucher and package labels to the external evaluator and updates TRIM accordingly.

18. The external evaluator carries out the evaluation and forwards his/her report (in both hard copy and electronic copy), invoice and the data to the Director, DSEB.

19. Upon receipt, the RMS forwards:

    a. the evaluation report together with a blue "Evaluation Report Authorisation" form and a copy of the invoice to the PCE senior evaluator (the report is placed on the relevant chem/biol file)

    b. the original invoice to the Finance Officer, and

    c. the returned data (which may arrive some days later) to the PCE senior evaluator and updates TRIM accordingly. (The data are placed in the senior evaluator's office or the PCE Compactus.)

20. The senior evaluator checks the report to ensure that it covers all of the data that were to be evaluated as stipulated in the contract and, if so, the PCE ASO (or the senior evaluator, if preferred) sends an acknowledgement letter to the external evaluator advising him or her that the report and data have been received.

21. The PCE senior evaluator reviews the report to ensure its completeness, referring to data where necessary, and prepares a file note which goes on the chem/biol file.

    In all cases the evaluator should write any required Section 31 letter to the sponsor and/or a summary for Australian Drug Evaluation Committee (ADEC).

22. Once the senior evaluator is satisfied that the report is acceptable, he or she completes and signs the "Evaluation Report Authorisation" form. [Note that this may be some weeks after the report is received. The senior evaluator should ensure that authorisation is completed as soon as possible to avoid any undue delay in payment of the external evaluator.]

23. The senior evaluator passes the relevant chem/biol file and the signed "Evaluation Report Authorisation" form to the PCE Section Head for counter-signature and formal authorisation of payment of the external evaluator.

24. The PCE Section Head forwards the original signed and countersigned Evaluation Report Authorisation form to the EAs and places a copy of the form on the chem/biol form which is then returned to the senior evaluator.

25. The EAs place a copy of the "Evaluation Report Authorisation" form on the coordination file and send a copy to the external evaluator for his/her information.

26. The EAs send: the original "Evaluation Report Authorisation" form, the signed purchase order form and a copy of the external evaluator's invoice to the DSEB Finance Officer together with the coordination file for processing of payment.

5. REFERENCES

Nil

6. ATTACHMENTS

Appendix - Schedule of target times for external evaluators

Appendix: Schedule of target times for external evaluations

The table below sets out the average times that the PCES has found from experience that evaluations of the different types of data (for non-biological medicines) that a reasonably experienced evaluator can reasonably be expected to require. The total time taken should be the sum of the times allocated for the different units of work involved.

Chemical and Pharmaceutical Data*

	Time in Hours
Type 1:	36
Type 2:	20
Type 3:	16
Extra dosage form (= Type 3):	16
Extra strengths:	3 (each)
Drug Master File (non-NCE):	8

Biopharmaceutic Data #

Type:	Basic level:	initial study:	14
		extra study:	8 (each)
	Intermediate level:	initial study:	20
		extra study:	12 (each)
	Complex level:	initial study:	26
		extra study:	16 (each)
Summary only:			2 (each)
Replies to biopharmaceutic data questions:			3-6
Pharmaceutical/chemical consideration of non-provision of biopharmaceutic data:			1

Notes

* **Type 1**: New chemical entity, full evaluation of synthesis, proof of structure and other aspects of the drug molecule is required together with evaluation of the data on the finished dosage form.

Type 2: Existing drug for generic, new strength, new dosage form etc where evaluation of a Drug Master File (DMF) is required together with evaluation of the dosage form data.

Type 3: Other applications involving an existing drug but where evaluation of a DMF is not required, e.g. a European Certificate of Suitability supplied or the product is a new strength of a recently registered new chemical entity where all details of the drug substance remain unchanged. Only the drug product is to be evaluated.

Basic level study: 2 treatments cross-over study with 1 analyte.

Intermediate level study: 2 treatments cross-over with 2 analytes or 3-4 treatments, cross-over/parallel study with 1 analyte.

Complex level study: 2-4 treatments, cross-over/parallel study, 2 or more analytes and 1 or 2 assay methods.