

Review protocol: Stability data for antimicrobials relevant to the OPAT setting**Aims**

To:

- Update a previous review documenting the publicly accessible stability data for antimicrobials relevant to the OPAT setting.¹
- Document stability data compliant with the 'Standard Protocol for Deriving and Assessment of Stability, Part 1 Aseptic Preparations (Small Molecules) in the OPAT setting.'²
- Identify studies that highlight instability as well as those that confer extended stability.

OPAT Stability Search Protocol

Databases: Medline, PubMed, EMBASE, CINAHL, BMJ Journals, Cochrane Database for citations in English published between October 2015 and December 2020.

Process Step	Keywords
#1	Anti-infective agents OR antibiotic OR antimicrobial OR antiviral OR antifungal OR aciclovir OR amikacin OR amoxicillin OR amphotericin OR ampicillin OR anidulafungin OR avibactam OR azithromycin OR aztreonam OR benzylpenicillin OR caspofungin OR cefazolin OR cefepime OR cefotaxime OR ceftazidime OR ceftazidime OR ceftriaxone OR ceftolozane OR cefiderocol OR cilastatin OR chloramphenicol OR clarithromycin OR clavulanic acid OR clindamycin OR co-amoxiclav OR colistimethate OR colistin OR dalbavancin OR daptomycin OR doripenem or ertapenem OR flucloxacillin OR fosfomycin OR fosfomycin OR fusidic acid OR ganciclovir OR gentamicin OR imipenem OR imipenem OR isavuconazole OR meropenem OR meropenem OR micafungin OR oritavancin OR piperacillin OR posaconazole OR relebactam OR streptomycin OR sulbactam OR tazobactam OR teicoplanin OR telavancin OR temocillin OR ticarcillin OR tigecycline OR tobramycin OR vancomycin OR vaborbactam
#2	Drug stability OR drug storage OR stability OR shelf life
#3	Syringes OR elastomeric OR drug delivery device* OR drug delivery system OR infusion OR continuous infusion OR extended infusion
#4	#1 AND #2 AND #3

Inclusion Criteria

- Investigation of formulation for intravenous administration
- Testing under relevant storage conditions e.g. refrigerated or room temperature followed by 'in-use' storage at a temperature greater than 30 °C for the duration of the infusion.
- At least 90%–110% of active pharmaceutical ingredient (API) and in compliance with BP standards if monograph suggest tighter limits to remain to confer stability.
- Use of a validated stability indicating assay, e.g. HPLC.
- Complete physical stability testing, e.g. physical appearance, pH, colorimetry, sub-visible particulate assessment.
- Identification and quantification of degradation products if limits on such are stated in the BP monograph
- At least three samples tested at each time point.
- Testing of low and high 'clinically significant' concentrations.
- All samples tested in duplicate.

Exclusion Criteria

- Studies that do not comply with the minimum data set of the 'Standard Protocol for Deriving and Assessment of Stability, Part 1 (Small Molecules).
- Antimicrobials with no role in the OPAT setting.

Two reviewers will independently screen articles for inclusion, discuss and resolve discrepancies, and undertake data abstraction. A third reviewer will arbitrate, if necessary.

Data abstraction and synthesis

Data of selected articles will be abstracted onto a customised data extraction sheet focusing on inclusion criteria and building on the categories included in the first review. Variables in the previous review included: author and year; title of the study; country of origin; temperature range; API range; design; number of samples and duplication. Additional variables we will seek to extract include: identification and quantification of degradation products and whether there are BP limits for these and any COVID-19 related findings.

Key findings from each study will be summarised and presented in tables. Reviewers will code the variables and resolve any disputes through mutual discussion and arbitration by a third reviewer if necessary.

References:

- 1 [Jenkins A, Hills T, Santillo M, Gilchrist M. Extended stability of antimicrobial agents in administration devices. *Journal of Antimicrobial Chemotherapy* 2017;72\(4\): 1217-20.](#)
- 2 [NHS PQAC Committee. Standard Protocol for Deriving and Assessment of Stability, Part 1 Aseptic Preparations \(Small Molecules\). Fifth Edition, 2019.](#)