

DRUG STABILITY – AN EVIDENCE REVIEW AND DEVELOPMENT OF A NATIONAL METHODOLOGY FOR STABILITY TESTING OF AGENTS AND DEVICES

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On behalf of the BSAC OPAT Standards Work-stream on Devices
Drug Stability and the Literature Review Working Group

Structure



- Prefilled and OPAT
- National Survey Results
- Literature Review
- BSAC Tender Project

OPAT Delivery and Drug Stability

- Self Administration
- IV infusion centre
- Healthcare worker delivered

Options for Self-administration

- Syringes, diluents and vials
- Bags, flow restrictors/pumps
- Pre-compounded syringes
- 24hr Syringe pumps
- Elastomeric devices

Pre-filled Devices

□ Syringes

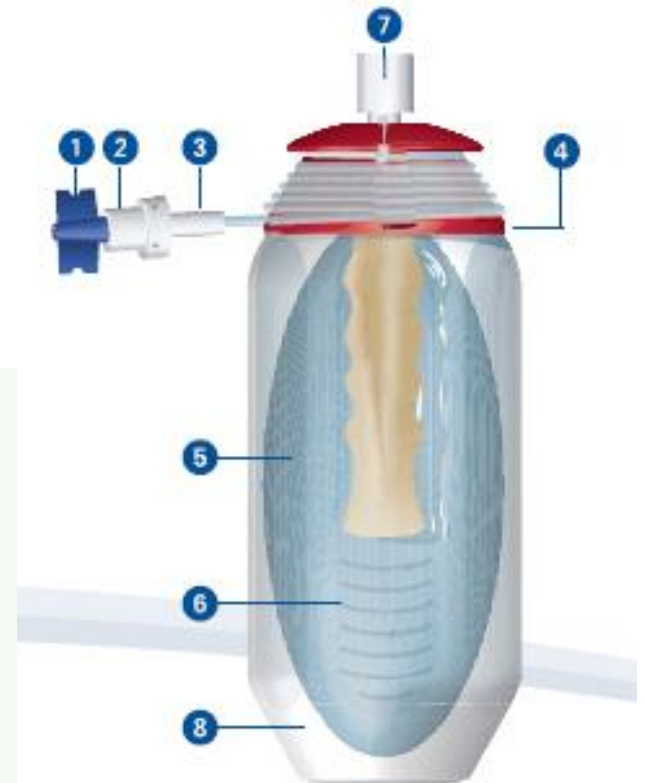
- Bolus and 24hr infusion

□ Elastomeric pump:

- Reasonable options of all OPAT drugs (inc. vancomycin).
- 24hr infusion option available



Large Volume Infusor
Small Volume Infusor

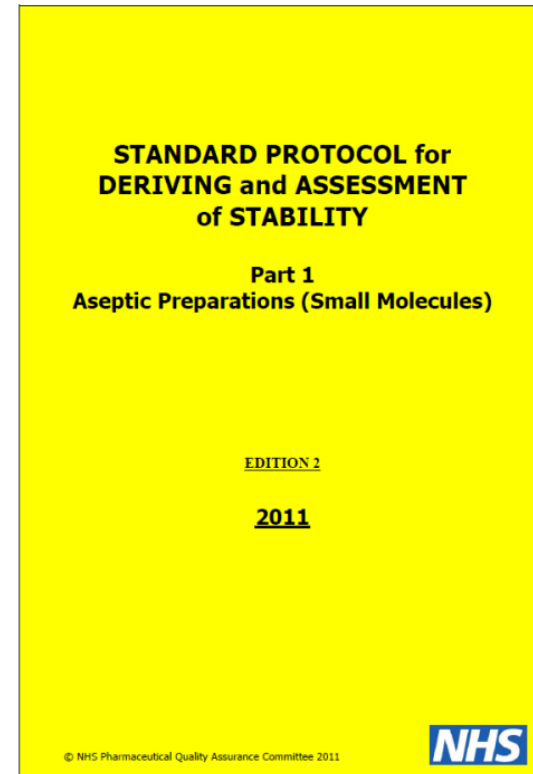


Obtaining prefilled devices

- Local pharmacy sterile production department
 - ▣ Under supervision of a pharmacist “special” (max 7 days)
 - Supply requires a registered pharmacy
 - ▣ Manufacturing licence (longer expiry but batch manufacturer and QC)
- Other NHS Trust production department
- Private/Homecare provider

“Appropriate” stability data

- “Special” licenced
 - ▣ Dependent on opinion of specialist production pharmacist.
- “Batch production”
 - ▣ Require manufacturers licence
 - ▣ In agreement with local QC department (National QC standards 2011).




The Problem


- General knowledge of the available stability data in the OPAT community is poor.
- Data often not published as commercially sensitive.
- BSAC Stability work-stream

BSAC OPAT Drug Stability in Devices work-stream

1. Survey which drugs/devices UK centres would be keen to use.
2. Review the literature around stability.
3. Undertake stability testing to national standards where gaps in the literature exist and publish in the public domain.



The British Society for
Antimicrobial Chemotherapy



OPAT
Outpatient Parenteral
Antimicrobial Therapy

Drug Stability & Testing in the OPAT Setting

Introduction

The BSAC OPAT Initiative has recently launched a new workstream to examine the topical area of drug stability in elastomeric devices and pre-filled syringes used in the OPAT setting. As part of this workstream, a review of the current evidence is being undertaken and will be available through the www.e-opat.com website.

To assist this particular workstream we would be grateful if you could complete this survey and provide as much information as possible regarding the drugs and devices that you currently use within the OPAT setting, as well as those you would consider using if stability information was available to you. This will direct future research undertaken by BSAC.

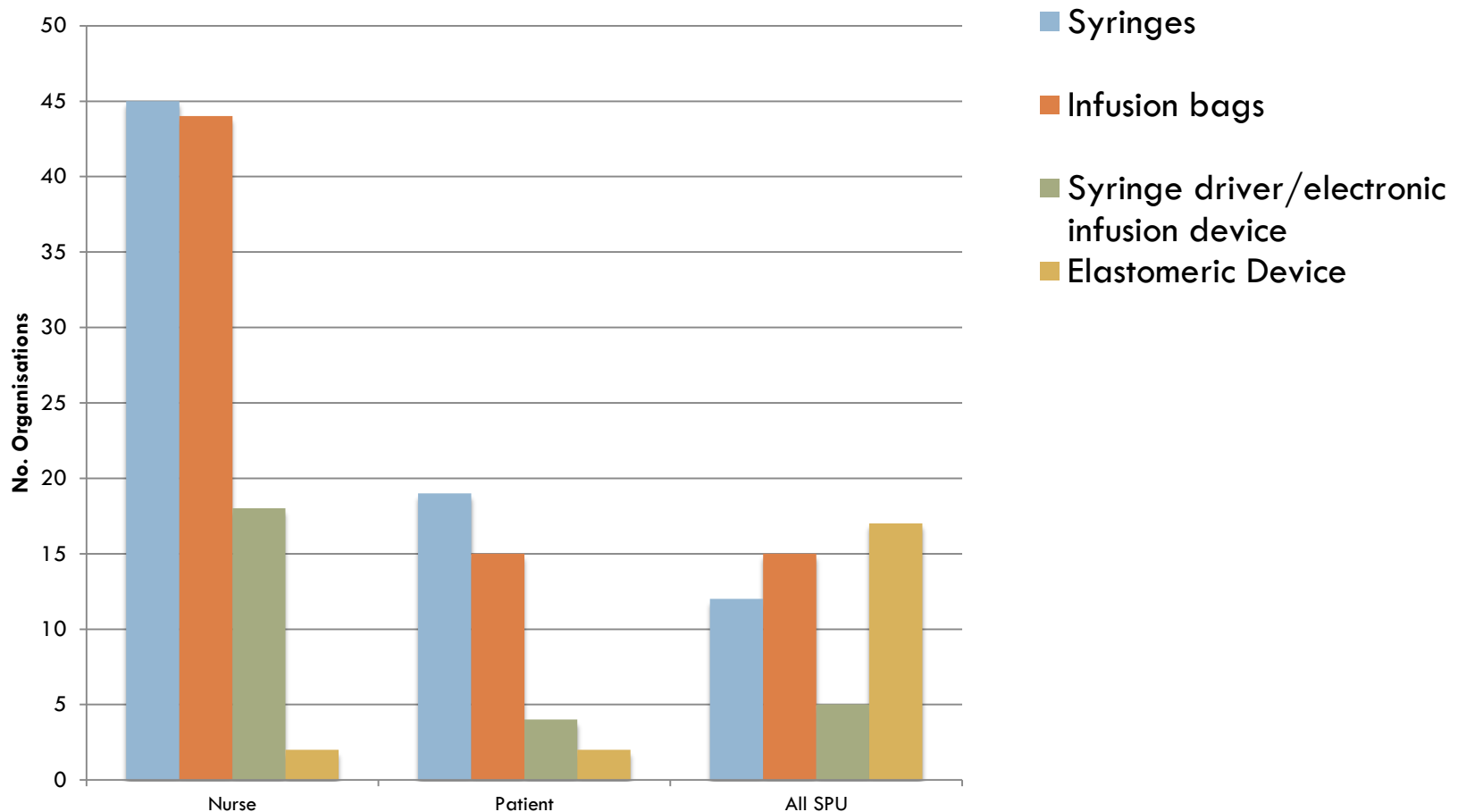
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Results of BSAC OPAT Stability Survey

- 120 responses from 52 Trusts
- In cases where multiple responses for a Trust were submitted
 - ▣ Compared, reviewed and amalgamated to produce one organisational response.
 - ▣ To amalgamate responses, each question was reviewed. If there was one or more positive response to a question the organisational response was marked as a positive.
 - ▣ Only if all responses were answered in the negative was the amalgamated response marked as negative.
 - ▣ All free-text comments were included in the organisational response.
- Final set of 52 survey responses for analysis.

Device and Method of Preparation of Antimicrobials Used in OPAT Services



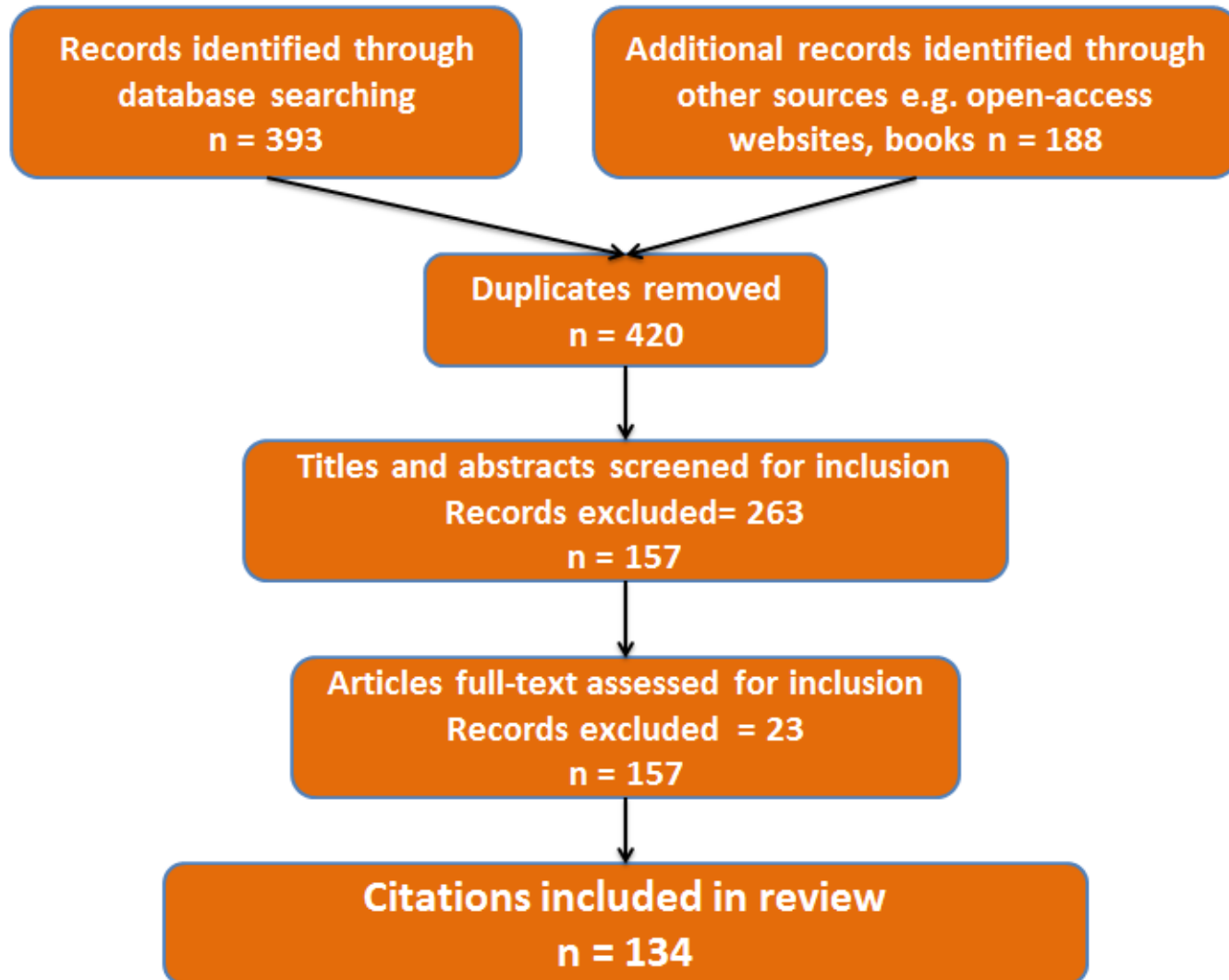
Drugs with Storage and/or Stability Data Reported by Organisations

Hospital	Pre-Filled Syringes		Elastomeric Devices	
1	-		Tazocin	
2	Ceftazidime Ceftriaxone	Colistin Tazocin	Ceftazidime Ceftriaxone Colistin Ertapenem	Meropenem Teicoplanin Vancomycin
3	Ceftriaxone Daptomycin	Meropenem Tazocin	Vancomycin	
4	Aztreonam Ceftazidime Ceftriaxone Colistin	Meropenem Teicoplanin Tobramycin	Amikacin Ceftazidime Ceftriaxone Colistin Ertapenem	Gentamicin Meropenem Teicoplanin Tobramycin
5	Ceftazidime Ceftriaxone Colistin Daptomycin	Meropenem Tazocin Tobramycin	Amikacin Aztreonam Ceftazidime Ceftriaxone Colistin	Flucloxacillin Meropenem Tazocin Tobramycin Vancomycin.
6	Ceftazidime	Ceftriaxone	Amikacin Ceftazidime	Ceftriaxone Vancomycin
7	Gentamicin		-	

Specific Antimicrobials that Organisations would like

- This slide is intentionally lacking detail!
- Due to current work programme can't give specific information
- However (and no surprise?!)
 - ▣ Around beta lactams
 - ▣ Narrow spectrum penicillins
 - ▣ Cephalosporins

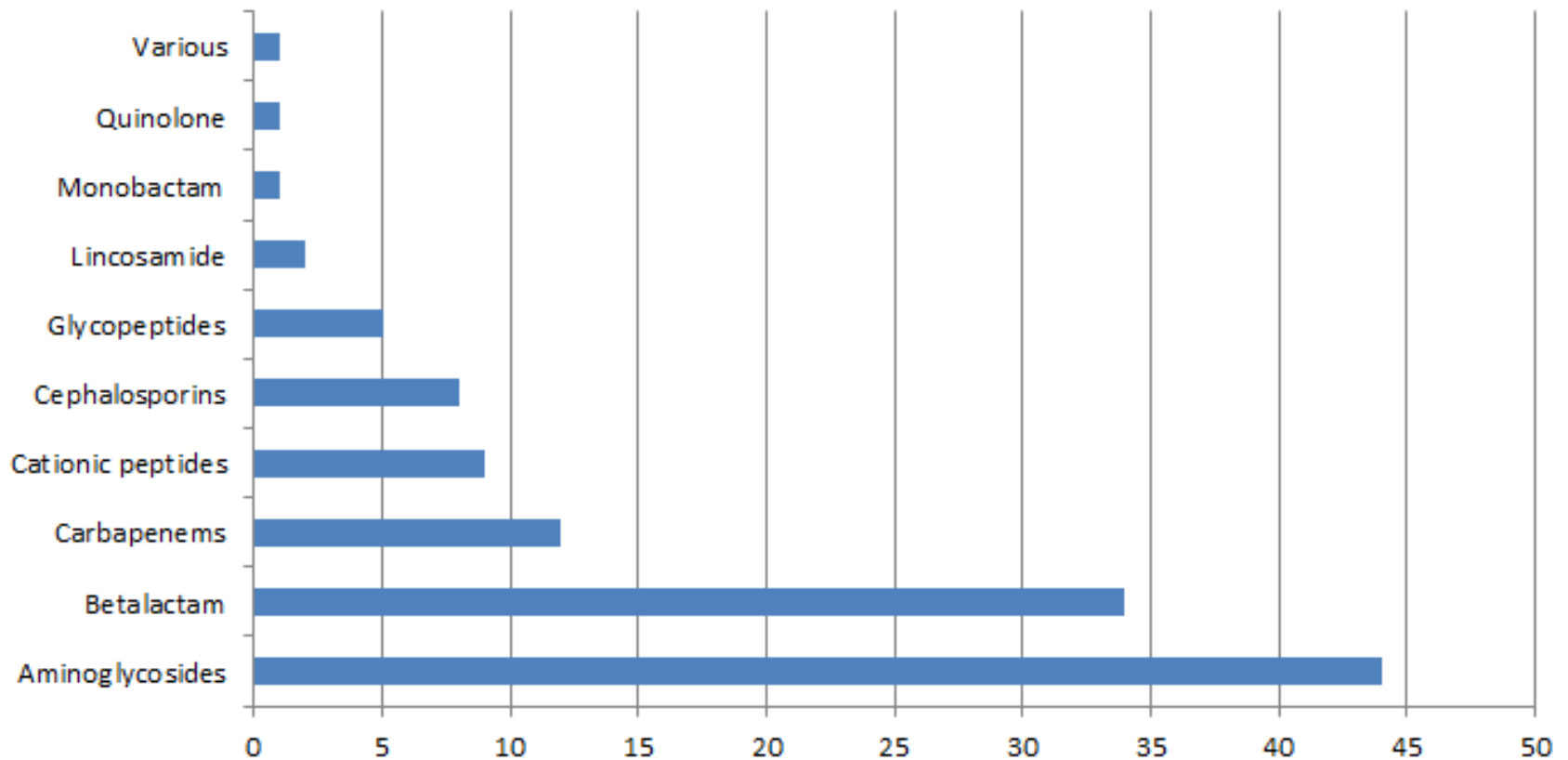
Available Papers



Literature Review

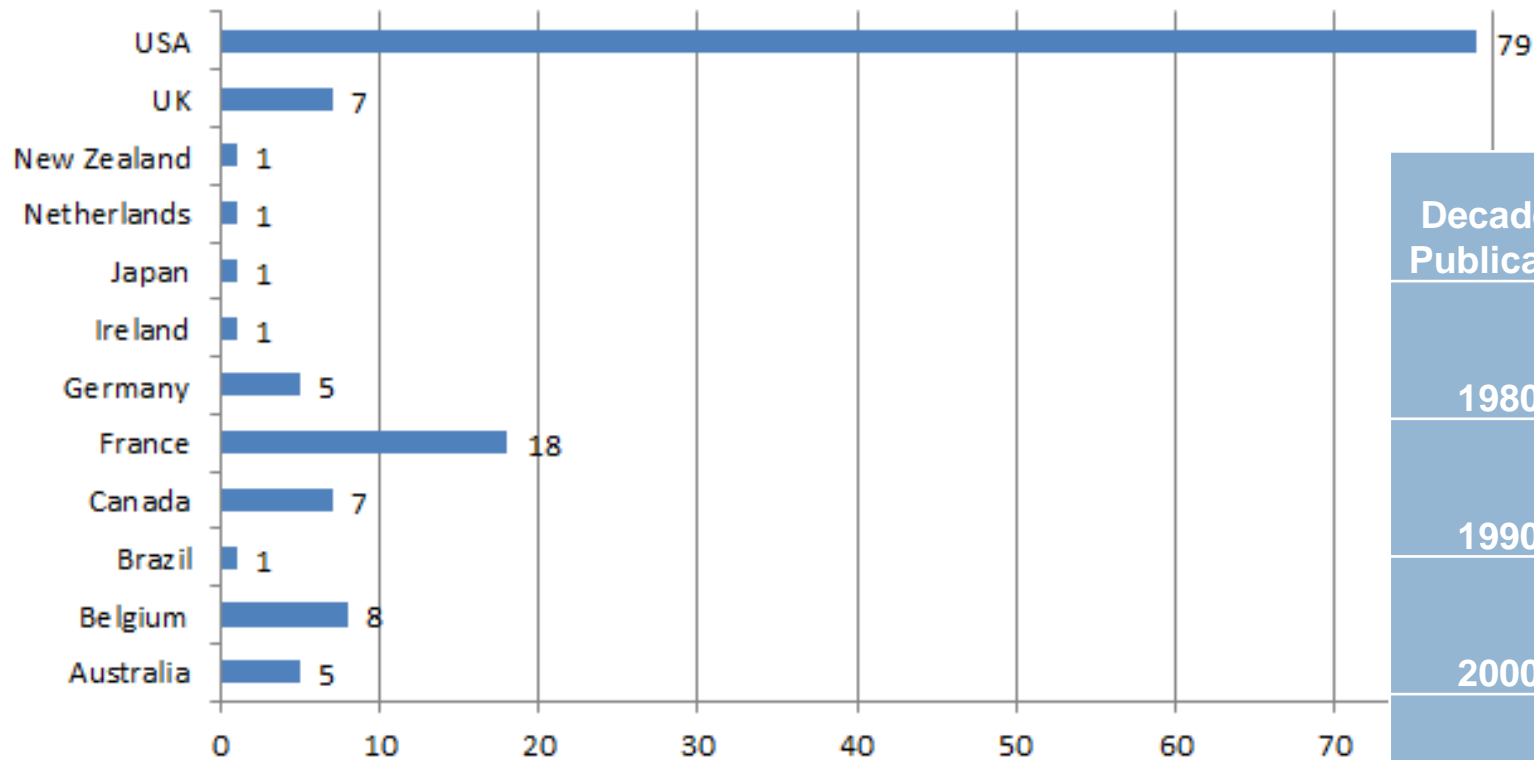
Articles by therapeutic Group

- 117 antibacterial 6 antifungal 11 antiviral



Literature Review

Articles by Country



Decade of Publication	No. Articles
1980s	25
1990s	55
2000s	38
2010s	16

Literature Review

**STANDARD PROTOCOL for
DERIVING and ASSESSMENT
of STABILITY**

**Part 1
Aseptic Preparations (Small Molecules)**

EDITION 2

2011

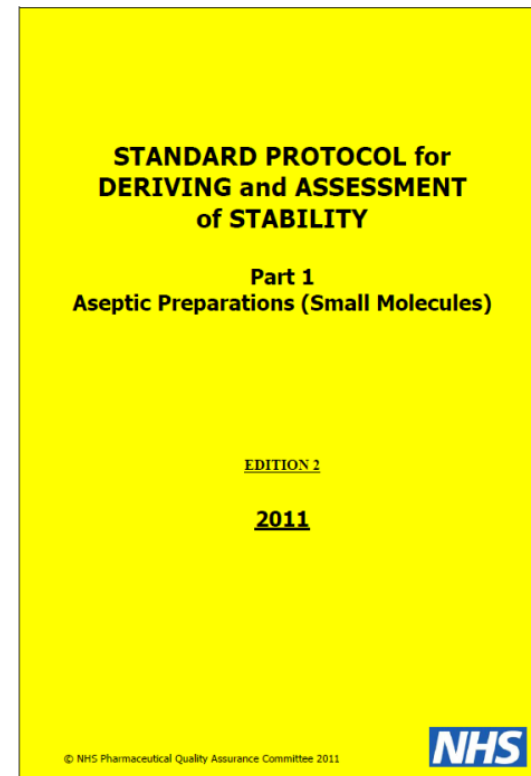
© NHS Pharmaceutical Quality Assurance Committee 2011



Paper:	Company name - Drug- concentration - presentation				Assessors, notes
	score				
Study parameter	0	1	2	3	
Study design - Diluents				3	Does the paper or report adequately define the preparation of the study samples including the diluents and/or additives used ?
Study design - containers			2		Does the report adequately describe the containers and closures used?
Study design - storage		1			Does the report describe the storage conditions? Are these in accordance with the YCD in terms of temperature/humidity / light?
Study design - replication	0				Has the study used a level of replication in line with the YCD?
Analytical method - test procedure		1			Is the choice of analytical technique appropriate and is there evidence of stability indication ? For chromatographic analysis- can we make a judgement on the chromatography and ability to resolve related compounds ? Are complimentary analyses (pH, particulate assessment, limit tests etc) adequately applied in line with the YCD ?
Analytical method Validation			2		Does the report describe method validation expected for a pharmaceutical study? (ICH Q2 is the general reference document).
Data processing				3	Does the report detail data at each time point and are the data presentations supported by appropriate statistical techniques in line with the YCD guidance ?

Literature Review

- None fully complied with the NHS QC Standards.
 - ▣ Too few samples and/or tests
 - ▣ Storage conditions esp. body worn
 - ▣ 10% vs 5% degradation
 - ▣ Investigation into degradation products
- Differences between UK and US standards
- Review/survey to be submitted for publication.



BSAC Drug Stability Tender

- Awarded service to start September 2015
- 2-4 OPAT related antimicrobials/year
- 2-3 years
- Includes syringes/bags/at least two elastomerics
- Including paediatric conc.
- Meropenem
- Flucloxacillin +/- Buffer



The screenshot shows the BSAC website header with the logo and navigation menu. Below the header is a large image of a person in a lab coat looking through a microscope. A social sharing bar is visible below the image. The main content area features a news article titled "BSAC Drug Stability Tender – applications invited" with a sub-heading "Tender Notice for the Supply of Drug Stability Testing (2015-2017)".

BSAC The British Society for Antimicrobial Chemotherapy

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Latest News

- BSAC audited accounts & AGM 2015 agenda
- New microbiology-focused grants available from the UK research councils
- BSAC collaborates with ICMID to deliver stewardship training in Bahrain
- BSAC Drug Stability Tender – applications invited**
- BSAC welcomes NICE Consultation on

BSAC Drug Stability Tender – applications invited

Tender Notice for the Supply of Drug Stability Testing (2015-2017)

Through the UK Outpatient Antimicrobial Therapy (OPAT) Initiative the British Society for Antimicrobial Chemotherapy (BSAC) has played an active role in supporting provision of OPAT services wherever the clinical need might exist.

A 2013 BSAC survey of OPAT practitioners identified access to antimicrobial stability data as one of barriers to service entry and expansion. In order to address this barrier and support the clinical community BSAC is commissioning stability testing of antimicrobial agents and administration devices used for OPAT.

All stability data produced as a result of this activity will be published on open access basis for all members of the healthcare community to access as required.

Acknowledgements

- BSAC OPAT Standards Committee - Devices/Drug Stability Work-stream
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