WHY DOES BAXTER INVEST INTO STABILITY DATA FOR ITS PUMP ?

Information available from a drug manufacturer (for example from the relevant SmPC) does not offer the needed stability data for a specific container.[1]

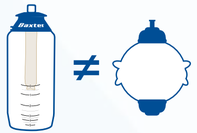
Published stability data may be of limited value because of inappropriate or inadequate analytical methodology, limited study duration or improper processing of analytical data.[1]

The shelf life should be subject to on-going validation including robust control of any changes to materials or components.[1]
A stability study is developed to establish a shelf-life for a specific drug compounded in Baxter's elastomeric pump.

IS BAXTER'S STABILITY DATA UNIQUE TO BAXTER'S ELASTOMERIC DEVICE ?

YES !

Stability studies are specific to the device tested and should not be extrapolated to other devices. When studying stability of a drug in a container, the drug behavior may be influenced by multiple elements, such as the contact material's adsorption properties.



WATER LOSS AND THEREFORE CONCENTRATION INCREASES WILL DIFFER BASED ON THICKNESS OF MATERIAL AND THE CASINGS.

Baxter's elastomeric material is made in our manufacturing plant using a unique proprietary formulation of polyisoprene rubber supplied by a trusted partner for more than 30 years.

STABILITY CAN BE AFFECTED BY ADDITIONAL FACTORS THAT COULD ALTER THE OUTCOME AND RELIABILITY OF THE DATA COLLECTED.

For example, the sterilization method may differ (i.e. gamma vs. EtO vs. steam) or may be done at a different level.
Baxter utilizes gamma irradiation to sterilize its elastomeric infusion devices.

[1] A STANDARD PROTOCOL for DERIVING and ASSESSMENT of STABILITY, Part 1 – Aseptic Preparations (Small Molecules), 3rd Edition December 2015, NHS Pharmaceutical QA Committee

WHICH DRUGS HAVE BEEN STUDIED WITH BAXTER'S ELASTOMERIC PUMPS ?

Over the last 30 years Baxter has developed stability data for more than 80 drugs used in its portable elastomeric pump.
Baxter is committed to keep investing in additional stability studies to reflect the evolution of practice and standards.

Baxter stability data have been developed and studied for the following drugs:

CHEMOTHERAPY			
5-FLUOROURACIL	CISPLATIN	IFOSFAMIDE + MESNA	TRASTUZUMAB
5-FLUOROURACIL + FOLINATE	CLADRIBINE	METHOTREXATE	VINBLASTINE
BEVACIZUMAB	DOXORUBICIN	NIVOLUMAB	VINCRISTINE
BLEOMYCIN	FLUDARABINE	OXALIPLATIN	VINORELBINE
CARBOPLATIN	Calcium Folinate (Leucovorin)	PAMIDRONATE	ZOLEDRONIC ACID
CETUXIMAB	GEMCITABINE	PERTUZUMAB	
ANTI-INFECTIVE			
ACICLOVIR	CEFOTAXIME	DAPTOMYCIN	MEROPENEM
AMIKACIN	CEFOXITIN	ERYTHROMYCIN	OXACILLIN
AMPHOTERICIN B	CEFTAZIDIME	FLUCLOXACILLIN	PENTAMIDINE
AZTREONAM	CEFTRIAXONE	FOSCARNET	PIPERACILLIN
BENZYLPENICILLIN	CEFUROXIME	FOSFOMYCIN	PIPERACILLIN + TAZOBACTAM
CEFALOTIN	CIPROFLOXACIN	GANCICLOVIR	TIGECYCLINE
CEFAZOLIN	CLINDAMYCIN	GENTAMICIN	TOBRAMYCIN
CEFEPIME	COLISTIMETHATE	IMIPENEM + CILASTATIN	VANCOMYCIN
PAIN MANAGEMENT			
BUPIVACAINE + FENTANYL	HEPARIN + HYDROMORPHONE	LEVOBUPIVACAINE	ROPIVACAINE
BUPIVACAINE + SUFENTANIL	KETOROLAC + MORPHINE	LIDOCAINE	TRAMADOL
BUPIVACAINE	KETOROLAC + TRAMADOL	MORPHINE + ROPIVACAINE	
CHLOROPROCAINE	KETOROLAC	MORPHINE	
OTHERS			
APOMORPHINE	HEPARIN	LEVOFOLINATE	PIRITRAMIDE
DEFEROXAMINE	KETOBEMIDONE	METAMIZOLE	TERBUTALINE
DESFERRIOXAMINE	LENOGRASTIM	ONDANSETRON	

This list was compiled in 2017. For additional stability data developed since then, please contact your local representative.

For the safe and proper use of this device, refer to the appropriate operator's manuals.
For any drug products dosing, preparation or use mentioned herein, please consult the Product Monograph or your facility's protocol.

Delivering flexibility, freedom and confidence

SG/MG33/20-0001

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Baxter
Infusor
AMBULATORY SYSTEMS

GENERATING
comprehensive
stability data

HOW ARE THE STUDIES BEING DESIGNED AND CONDUCTED ?

For more than 30 years, Baxter has developed proprietary know how to generate stability data for drugs used with Baxter's elastomeric pumps.

Stability studies are conducted under Baxter R&D responsibility. Such operating model allows for standardized methodology across studies and therefore consistent quality of the studies.

The following steps highlight Baxter's approach to conducting stability studies.

1. COLLECT THE STUDY REQUEST

Study requests from customers are collected by the field team.
Study requests are centralized globally and follow a process of prioritization.

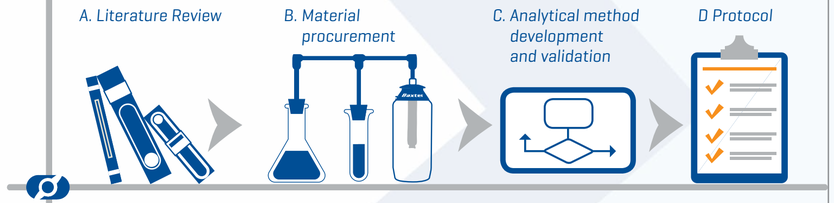
The data needed to proceed is:

- ✔ **The desired shelf life** for the molecule. For example 14 days at 2-8°C (storage in the fridge) followed by 7 days at 33°C (allowing the use of a Sevenday Infusor at body temperature as per NHS guidelines[1]).
- ✔ **The drug concentration**
- ✔ **The drug brand**

[1] A STANDARD PROTOCOL for DERIVING and ASSESSMENT of STABILITY, Part 1 – Aseptic Preparations (Small Molecules), 3rd Edition December 2015, NHS Pharmaceutical QA Committee

2. DEVELOP THE STUDY

The study request is then handed to Baxter's R&D team who will start by developing the study and assessing its feasibility.



A. LITERATURE REVIEW

The R&D team performs a literature review to consolidate known pertinent information of the molecule at the time of the study in order to:

- ✔ Assess request feasibility
- ✔ Define the analytical strategy

B. MATERIAL PROCUREMENT

The R&D team then proceeds with material ordering.
The materials used to conduct the study consist of sterile products: the drug(s), the diluent and the elastomeric device.
In most cases, two diluents are tested, i.e. 0.9% NaCl and 5% dextrose.
In the case of lyophilized powder, a reconstitution fluid may be used before subsequent dilution with appropriate diluent.

C. ANALYTICAL METHOD DEVELOPMENT AND VALIDATION

The R&D team demonstrates the performance of the stability indicating analytical method against intended purpose by assessing a series of validation parameters amongst which linearity, precision and accuracy.

D. PROTOCOL

The resulting stability study protocol includes detailed information of the drug that is studied (supplier, country of origin, number of batches), the concentration range (matrix approach)*, and the devices. The protocol furthermore includes clear directions based on the insert sheet and common European Hospital Pharmacy practices towards the reconstitution and dilution of the drug.

* Baxter uses the matrix design as the alternative design to the full testing approach. The matrix design allows to apply shelf-lives within a range of concentrations.

3. CONDUCT THE STUDY

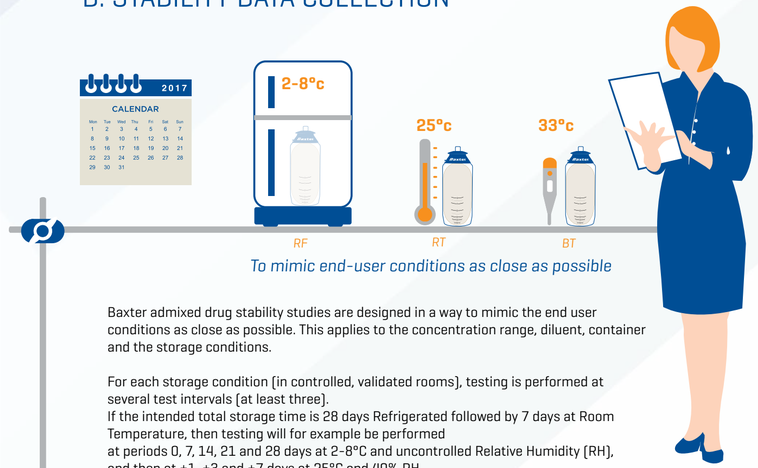
The Stability study can now be conducted with special care for the following steps.

A. RECONSTITUTION AND DILUTION

The drug is reconstituted and diluted (if needed), in a biological safety cabinet to protect both the product and the operator.

To guarantee the microbiological quality over the given shelf life, a strict aseptic technique during compounding is applied (as described in ICH, CPMP, USP or other normative references).

B. STABILITY DATA COLLECTION



To mimic end-user conditions as close as possible

Baxter admixed drug stability studies are designed in a way to mimic the end user conditions as close as possible. This applies to the concentration range, diluent, container and the storage conditions.

For each storage condition (in controlled, validated rooms), testing is performed at several test intervals (at least three).
If the intended total storage time is 28 days Refrigerated followed by 7 days at Room Temperature, then testing will for example be performed
at periods 0, 7, 14, 21 and 28 days at 2-8°C and uncontrolled Relative Humidity (RH), and then at +1, +3 and +7 days at 25°C and 40% RH.

Tests performed at each interval include visual inspection (to detect color change or appearance of visible particulate matter), and measurement of pH and drug content.
In certain cases, impurities and degradation products are also determined if applicable.

C. STATISTICAL ANALYSIS

At the end of the study, stability results and/or statistical analysis provides objective evidence supporting calculated shelf life. The applied limits can either be the pharmacopeial limits (BP, USP) for active as well as for degradation products or in-house drug content limits when no monograph exists.

D. STUDY CONCLUSIONS

Upon stability study conclusion, the stability data are posted on **stabforum.baxter.com**, a password protected platform available to healthcare professionals. Healthcare professionals can request access on the login page.

The stability information is a compilation of specific, experimental data that have been generated to the common standard practices at the time of the study. It does not support the effectiveness of the dosages quoted. The shelf lives indicated are valid for admixtures prepared using strict aseptic technique. It is not intended to replace the professional judgement of the caring physician, pharmacist or other qualified healthcare professional. Qualified professionals should pay attention to drug manufacturers recommendations and claims to establish their judgement.

The app is also available under "Basecase"

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