

A comprehensive guide, covering all your bases.





# There's a lot of misconceptions when it comes to beyond-use-dating.

MYTH: Potency over time studies alone are sufficient evidence for extending a BUD

FACT: Stability-indicating goes beyond potency. Potency testing was used in the past, however stability-indicating is the correct way of conducting a BUD study.

Potency refers to the concentration of the drug at a specific point in time. It only indicates how much of the medication is present in a compound.

Stability-indicating studies ensure the durability of the compound over time and separate the drug from its by-products to get a more accurate picture of the amount of medication present.

MYTH: Physical Compatibility = Chemical Stability

FACT: Just because it looks good, doesn't mean it is good.

Physical compatibility doesn't tell the whole story. Chemical stability allows to look beyond the surface of the compounded preparation. MYTH: Pharmacists are limited to purchase materials from one compounding vendor in order to apply extended BUDs

FACT: Threatening disclaimers restricting the use of compendial grade materials, such as APIs and excipients, have been used as a marketing tactic.

Unlike bases, most actives are not proprietary or unique. An extended BUD is formula specific, and does not require the API to originate from a specific source. Pharmacies have the ability to qualify other suppliers for these products.

This is evident when looking at a USP compounded monograph where the supplier is specified for the base, but not the API.

MYTH: Bracketed studies are a requirement

FACT: They are helpful and good to have, but not a requirement for extending a BUD.

# STAY INFORMED.



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### What are BUDs (Beyond-Use Dates)?

The BUD is the date or time, after which a compounded preparation can no longer be used, administered or stored, and is determined from the date the preparation is compounded.



#### How do you establish a BUD?

- USP, NAPRA and APF have set forth guidelines for establishing beyond-use-dating of compounded preparations.
- Compounders should take into consideration the properties of the API(s), any excipients, the type of dosage form as well as container closure and storage conditions.
- Establishing the BUD of a compounded preparation should be based on concrete scientific data.
- The correct way to obtain an evidence-based extended BUD is by conducting a stability-indicating study.
- In the absence of supporting stability data, pharmacists refer to USP <795>, NAPRA or APF guidelines.



## Why are BUD studies important?

- BUD studies are stability studies that help to ensure the integrity of the compounded preparation is maintained using validated, stability-indicating methods.
- They diminish potential risks that can affect patients, such as degradation of the active which can alter potency as well as **safety** due the formation of potentially dangerous by-products over time.
- A BUD study determines whether a preparation is able to maintain its strength and properties throughout its period of preparation, storage and use and to protect itself from degradation over time.
- BUD studies also allow compounders to extend the dating of compounded preparations beyond the default guidelines.
- In compliance with PCAB requirements for extending BUDs.



## What are the advantages of having an extended BUD?

#### Benefit the patient by:

- Increasing the accessibility of medically necessary treatments (ex. patients living far from a pharmacy, vacations).
- Reducing prescription renewal frequency and in turn reducing costs.
- Offering more peace of mind in receiving a compounded preparation.

#### Benefit the pharmacy by:

- Improving pharmacy workflow.
- Reducing costs by reducing labor (due to improved workflow), compounding larger batches and saving on shipping.
- Providing the opportunity to prepare stock preparations.

# What you don't know, can hurt you...



## BUDs are much larger than they seem:

Stability-Indicating Studies are the gold standard for BUDs.

#### What is a stability-indicating study?

- A stability-indicating study consists of a validated, quantitative, analytical procedure used to detect how the stability of a drug changes over time.
- Stability-indicating assays can use techniques such as HPLC, MS, LC-MS/MS.
- A stability study includes:
  - Method development
  - Method validation
  - Forced degradation study

#### **Forced-degradation**

- Exposing the compound to extreme conditions (heat/humidity/uv radiation/acids/bases).
- Separating the drug from degradant.
- Determining quality and durability of a compounded preparation.

# How do you determine you have a good stability-indicating study?

- Stability-indicating assays
- Validated methods
- Statistical analysis
- Independent & objective results
- Published and peer-reviewed (bonus!)
- Bracketed (bonus!)

#### What is a bracketed study?

- The study of two concentrations of a specific API or formulation in the same base, container closure system and under the same storage conditions.
- The only variable is the difference in concentration of the drug all other factors remain consistent throughout both studies.

# **Oral & Topical BUD Databank**

Determined Using Stability-indicating Studies

(C) = Controlled substance in US and Canada **ORAL MIX** BUD FORMULAS 🛝 API Sulfamethoxazole/Trimethoprim 90 days at 5°C and 25°C F 007 892v3 40/8 mg/mL 90 days at 4°C and 25°C F 006 379 Levetiracetam 50mg/mL \* Melatonin 2.0mg/mL 90 days at 4°C and 25°C F 006 112 Gabapentin 100mg/mL 90 days at 25°C F 006 620v2 Product No.: 2512 FORMULAS 🚵 **ORAL MIX SF** API BUD Sulfamethoxazole/Trimethoprim 90 days at 5°C and 25°C F 007 893v3 0/8 mg/mL Metronidazole 50mg/mL 90 days at 4°C and 25°C F 007 000 Dexamethasone 1mg/mL \* 90 days at 4°C and 25°C F 006 625v3 90 days at 25°C F 006 621 Gabapentin 100mg/mL Product No.: 2600 VERSAPRO<sup>™</sup> CREAM API BUD FORMULAS 🎪 DHEA 0.2%-4%, Estradiol 0.01%-0.2%, 180 days at RT and Estriol 0.04%-0.8%, Progesterone 1%-20%, F 008 949 ongoing Testosterone 0.025%-0.5% (Bracketed) C VERSAPRO 180 days at RT and LOT 12 DOT 01 Diclofenac Sodium 1%-15% (Bracketed) F 008 945 ongoing Product No : 2529 Progesterone 1%-40% (Bracketed) 180 days at RT F 008 567 FORMULAS 🚵 HRT CREAM BUD API DHEA 0.2%-4%, Estradiol 0.01%-0.2%, 180 days at RT and Estriol 0.04%-0.8%, Progesterone 1%-20%, F 008 948 ongoing Testosterone 0.025%-0.5% (Bracketed) C HRT CREAM BASE F 008 950 Hydroquione 2%-10% (Bracketed) 60 days at RT and ongoing COSE BYOST-ONE COSE BUCK STUDION Estriol 0.01%-10% (Bracketed) 180 days at RT F 008 331 Product No.: 0701

\* Preparation compounded using commercial drug product (e.g., tablet, capsule, sterile powder for injection)

# Explore our FULL BUD databank with 70 FREE FORMULAS www.medisca.com/BUD

DISCLAIMER: This data is provided for informational purposes only, representing the results of a study of the product stability with various active pharmaceutical ingredients. For further information on packaging, please refer to the actual formula. This document does not serve, and may not be construed, as a representation or guarantee of product performance. In all cases the practitioner is advised to consult recognized pharmaceutical compendia and other recognized sources for product formulation and other product characteristics, including stability. MEDISCA and its affiliates make no warranties or representations with regards to the functioning or appropriateness of this product in any compounded formulation, the use of which is solely at the discretion and liability of the practitioner. It is the responsibility of the pharmacist or other appropriately state licensed professional to verify the accuracy and validity of the information contained herein, with regards to scheduling, federal and state/provincial laws allowing the use of the formulas, products and final compounds in the country of use.

# **MEDISCA & BUDs**

# We keep your patients' health and safety our first priority, by

- Investing in best practices
- Contracting 3rd party institutions to conduct our studies
- Studying multiple batches for reproducibility
- Publishing results in peer-reviewed journals
- Setting and exceeding industry standards

#### Keeping pharmacists top of mind

We developed bracketed BUD studies to provide the best resources for your practice, giving you flexibility to use our extended BUDs for a wide range of concentrations.

- Single API studies at both low and high concentrations, facilitating larger batches for improved workflow and efficiency
- Various combinations with commonly used HRT actives for added confidence and assurance

# **Quality + Quantity**

We have invested in quality, and now we are committed to providing more studies this year: In 2020, we have invested in over 20 new stability-indicating studies www.medisca.com/BUD



In keeping up with industry trends and the ever-changing regulatory landscape, we have reformulated:



HRT CREAM BASE Removed Parabens



VERSAPRO™ GEL BASE

Removed Methylisothiazolinone/ Methylchloroisothiazolinone



VERSAPRO™ CREAM BASE

Removed Methylisothiazolinone/ Methylchloroisothiazolinone





- Specially developed to achieve a water activity below 0.6, allowing for extended 180 day default BUDs, as per current USP <795> guidelines.
- Scientifically formulated to contain several ingredients to promote drug delivery of both lipophilic and hydrophilic APIs providing compounders the versatility they need.
- The combination of silicone and natural oils provide the ideal patient sensory experience: a soft and moisturizing texture.

Available in a variety of sizes 50, 100, 500 g and 2.5, 5 and 20 Kg



www.medisca.com/versaproanhydrous

# FOR MORE INFORMATION USA 1-800-932-1039 | WWW.MEDISCA.COM/BUD

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