STABILITY RESULTS OF EPINEPHRINE SUBLINGUAL FILM UNDER EXTREME TEMPERATURE CONDITIONS

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INTRODUCTION

- Epinephrine, administered intramuscularly into the anterolateral thigh via manual injection or auto-injector (e.g., EpiPen®, Auvi-Q®), is the first-line treatment for anaphylaxis.[1]
- Currently, all approved therapies involve delivery of an aqueous-based solution containing the needed epinephrine. Aqueous environments have known limitations when considering extreme temperatures.
- Therefore, an ideal epinephrine rescue medication for anaphylaxis should possess physiochemical properties that aid in withstanding environmental conditions that may occur during normal patient carriage, while not sacrificing shelf-life. For example, the product should retain sufficient chemical stability after exposure to a variety of real-world scenarios, such as the environmental conditions that can occur in a car, a pocket, a wallet, and when storing in a phone case.
- Anaphylm (AQST-109, DESF), is a sublingual film containing a prodrug of epinephrine, in development as a non-device, minimal water containing alternative to address the limitations associated with all currently approved therapies.

OBJECTIVES

- To evaluate the stability of Anaphylm under extreme temperature conditions (50°C, 60°C, and 70°C) and its impact on potency and quality over 12 months.
- To assess the long-term stability of Anaphylm at ICH storage conditions (25°C/60% RH, 30°C/65% RH, and 40°C/75% RH) post-exposure.
- To evaluate the retention of critical quality attributes post-exposure to elevated temperatures.

METHODS

STUDY DESIGN

- This study evaluated the stability and performance of, or impact on, the drug's packaging and chemical integrity under simulated real-world conditions.
- The product was subjected to a series of simulated high-temperature exposures,
- After the temperature excursions, the films were returned to room temperature and tested for critical quality attributes to assess for degradation.
- Subsequently, the films were stored for 12 months under ICH conditions (25°C/60% RH) to further evaluate their stability over time.
- Anaphylm was exposed to:
  - 50°C for 28 days
  - 60°C for 21 days
  - 70°C for 7 days
- Potency and critical attributes were tested post-excursion and monitored for up to 12 months at standard storage conditions.

Anaphylm demonstrates robust stability across a wide range of temperature exposures to potentially support varied patient lifestyles.

CONCLUSIONS

- Anaphylm retains stability across a wide range of temperatures, supporting use in real-world conditions.
- After extreme temperature excursions, Anaphylm maintains a greater than 12-month shelf life under ICH storage conditions.
- These results, in conjunction with freeze-thaw durability data (see Poster 304), underscore the potential durability of Anaphylm.
- These data support the potential for Anaphylm to function in alignment with environmental conditions common in patient's lives.

RESULTS

STABILITY UNDER EXTREME TEMPERATURES

- Potency results (**Table 1**):
  - 50°C for 28 days: Potency retained at 97.7% initially and 96.9% after 12 months.
  - 60°C for 21 days: Potency retained at 97.3% initially and 95.2% after 12 months.
  - 70°C for 7 days: Potency retained at 96.6% initially and 91.7% after 12 months.

CRITICAL QUALITY ATTRIBUTES

- Dissolution and physical integrity remained within specification after temperature excursions (**Figure 1** and **Figure 2**).

Table 1: Anaphylm Potency – Control and Post-Temperature Excursion Followed by ICH Stability

Assay % LC				
Excursion Duration	Excursion Condition			
	No Excursion	50°C	60°C	70°C
T0	100.8%	102.2%	102.2%	102.2%
1 Week	---	---	101.6%	96.6%
2 Weeks	---	97.2%	99.7%	---
3 Weeks	---	96.7%	97.3%	---
4 Weeks	---	97.7%	---	---
Stability Time Point	ICH Stability @ 25°C/60% RH	Post Excursion ICH Stability @ 25°C/60% RH		
3M	99.9%	94.7%	94.4%	94.6%
6M	96.3%	93.9%	90.9%	92.3%
9M	97.6%	92.9%	91.3%	90.1%
12M	102.3%	96.9%	95.2%	91.7%

RESULTS (cont'd)

Figure 1: Anaphylm Potency – Comparison for Control and Post-Temperature Excursion Followed by ICH Stability

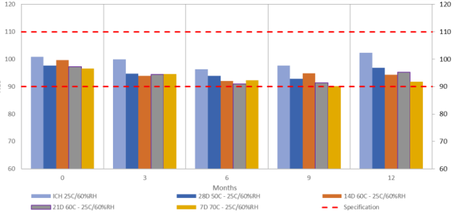
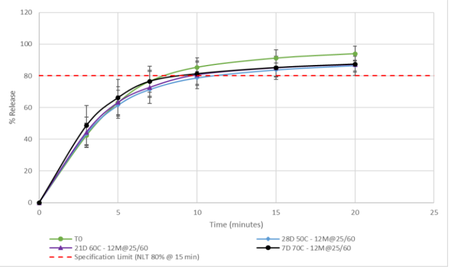


Figure 2: Anaphylm Release – Comparison for Control and Post-Temperature Excursion Followed by ICH Stability



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1. Shaker MS, Wallace DV, Golden DBK, et al. *J Allergy Clin Immunol.* 2020;145(4):1082-1123.

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DISCLOSURES

All authors are employees of Aquestive Therapeutics Inc.