

Stability of Epinephrine Nasal Spray under Freeze, Thaw, and Extreme Temperatures

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RATIONALE

- Severe allergic reactions typically occur outside healthcare settings and require patients and caregivers to respond quickly to avoid serious complications.
- To be rapidly accessible in any location, it is vital that epinephrine delivery devices be able to withstand a wide range of environmental conditions, including extreme temperatures.
- The stability of an epinephrine nasal spray 2 mg was evaluated during freeze/thaw cycles and following extended exposure to extreme heat.

METHODS

- Epinephrine nasal spray 2 mg samples were subjected to five consecutive 24- to 72-hour freeze/thaw cycles ranging from freezing (-20°C/-4°F) to extreme heat (40°C/104°F).
- Heat stability was also assessed relative to other epinephrine products, including autoinjectors and pre-filled syringe devices for community use. Products were kept at 50°C/122°F for 3 months or 40°C/104°F for 6 months, with a reference condition of 25°C/77°F.

RESULTS

ROOM TEMPERATURE CONDITIONS (25°C/77°F)

- Comparative potency for all products across room temperature conditions are provided in [Table 1](#).
- Potency for three lots of epinephrine nasal spray 2 mg under room temperature conditions are provided in [Figure 1](#).

FREEZE/THAW CYCLES (-20°C/-4°F to 40°C/104°F)

- Following the five freeze/thaw cycles, epinephrine nasal spray 2 mg potency ranged from 103.6% (Day 2) to 103.3% (Day 14) of labeled potency ([Table 1](#)).

EXTREME TEMPERATURE CONDITIONS (40°C/104°F and 50°C/122°F)

- Comparative potency for all products across extreme temperatures conditions are provided in [Table 1](#).
- After 6 months at 40°C/104°F, potency decreased by 27.5% for autoinjectors, 17.2% for pre-filled syringe devices, and 13.9% for epinephrine nasal spray 2 mg ([Figure 2](#)).
- After 3 months at 50°C/122°F, potency decreased by 56.6% for pre-filled syringe devices, 41.6% for autoinjectors, and 8.6% for epinephrine nasal spray 2 mg ([Figure 3](#)).

Table 1: Comparative Potency by Temperature Condition and Product

Duration (months)	Potency % under Room Temperature Conditions (25°C/77°F)		
	Epinephrine Nasal Spray	Autoinjector	Pre-filled Syringe Device
Initial	112.27	107.1	108.9
6 Months	107.7	102.2	98.9
Duration (days)	Potency % under Freeze-Thaw Conditions (-20°C/-4°F to 40°C/104°F)		
	Epinephrine Nasal Spray	Autoinjector	Pre-filled Syringe Device
Initial	104.7		
2 Days	103.6		
7 Days	102.8		
14 Days	103.3		
Duration (months)	Potency % under Heat Conditions (40°C/104°F)		
	Epinephrine Nasal Spray	Autoinjector	Pre-filled Syringe Device
Initial	106.7	107.1	108.9
1 Month	104.1	103.1	99.0
2 Months	100.6	98.2	91.2
3 Months	101.2	94.4	95.4
6 Months	92.8	79.6	91.7
Duration (months)	Potency % under Extreme Heat Conditions (50°C/122°F)		
	Epinephrine Nasal Spray	Autoinjector	Pre-filled Syringe Device
Initial	106.7	107.1	108.9
0.233 Month	104.2	104.5	105
0.5 Month	103.6	101.5	96.1
1 Month	102.6	96.7	79.2
2 Months	98.1	81.4	54.7
3 Months	99.0	65.5	52.3

CONCLUSIONS

- Epinephrine nasal spray potency was not meaningfully affected by multiple extreme freeze/thaw temperature fluctuations (-20°C/-4°F to 40°C/104°F) or by extreme temperature conditions after 3 months at 50°C/122°F or 6 months at 40°C/104°F, while autoinjectors showed a 27.5% to 41.6% loss in potency.
- Epinephrine nasal spray 2 mg is unlikely to have reduced efficacy following exposure to extreme high or low temperatures that mimic real world exposures, boosting confidence in use throughout its 24- to 30-month shelf-life. Patients and caregivers should always carry two devices with them.

Figure 1: Potency (%) Over Time at 25°C/77°F – Epinephrine Nasal Spray Lots

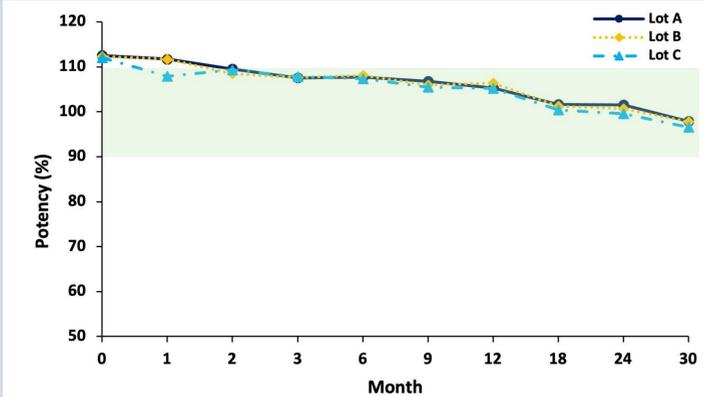


Figure 2: Potency (%) Over Time at 40°C/104°F

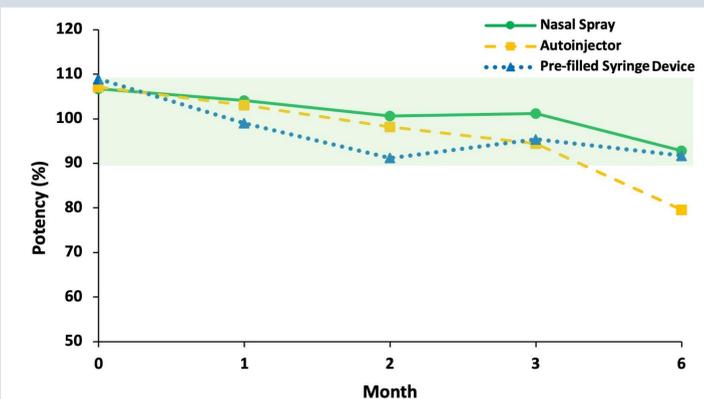
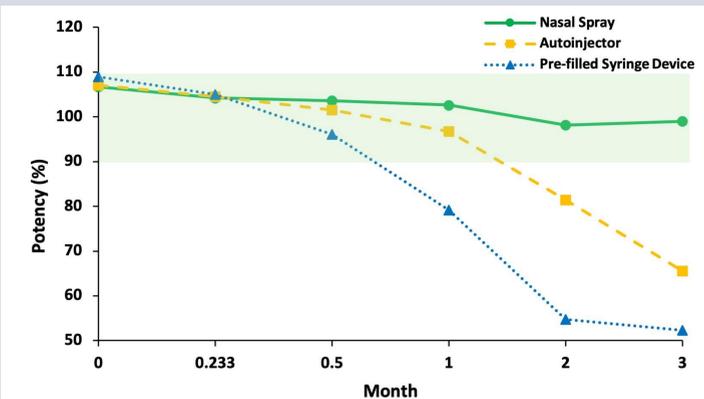


Figure 3: Potency (%) Over Time at 50°C/122°F



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