

## RESEARCH DOSAGE MANUAL

# MOTS-c FlexPen

Mitochondrial-Derived Peptide · 20 mg / 3 ml · Research Grade

*AMPK pathway activator — Manufactured in the Netherlands under cGMP*

<b>INN / Code</b>	MOTS-c (Mitochondrial Open Reading Frame of the Twelve S rRNA type-c)
<b>CAS Number</b>	1627580-84-0
<b>Class</b>	Mitochondrial-Derived Peptide (MDP) · AMPK Activator
<b>Molecular Weight</b>	~2,174.5 Da (16 amino acids)
<b>Concentration</b>	20 mg / 3 ml cartridge — 6.667 mg/ml
<b>Pen Dose Scale</b>	1 unit = 0.01 ml = 0.0667 mg (66.7 µg)   15 units = 1 mg   30 units = 2 mg
<b>Total Pen Doses</b>	300 units per cartridge (20 mg total)
<b>Purity</b>	≥ 99.0% HPLC · Endotoxin < 1 EU/mg
<b>Storage</b>	2–8 °C (36–46 °F) · protect from light · do not freeze
<b>Batch / Expiry</b>	NL-2026-MC · Expires 10/2028
<b>Administration</b>	Subcutaneous injection (research)

## 1. Compound Overview

MOTS-c (Mitochondrial Open Reading Frame of the Twelve S rRNA type-c) is a 16-amino acid mitochondrial-derived peptide (MDP) encoded within the 12S rRNA gene of the mitochondrial genome. First identified and characterised by Lee et al. (2015) at the University of Southern California, MOTS-c represents a novel class of bioactive peptides originating from the mitochondrial genome rather than the nuclear genome, establishing it as a fundamentally unique regulatory signal in cellular metabolism.

Circulating MOTS-c levels decline significantly with age and metabolic disease, and are inversely correlated with insulin resistance and obesity in human population studies. MOTS-c translocates to the nucleus in response to metabolic stress, where it directly regulates gene expression involved in glucose and lipid homeostasis. The VitalPep Pro formulation delivers research-grade MOTS-c at 6.667 mg/ml in a pre-filled FlexPen cartridge for precise, protocol-ready subcutaneous administration.

Reference: Lee C, et al. *MOTS-c: A mitochondrial-derived peptide regulating muscle and fat metabolism*. Cell Metab. 2015;21(3):443-454. Also referenced via [peptidedosages.com/mots-c/](http://peptidedosages.com/mots-c/) for research dosing protocols.

## 2. Mechanism of Action

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MOTS-c exerts its metabolic effects primarily through activation of AMP-activated protein kinase (AMPK), the master cellular energy sensor, and through direct nuclear gene regulation during metabolic stress. Key mechanisms include:

- **AMPK pathway activation:** MOTS-c activates AMPK by increasing the AMP:ATP ratio and through direct interaction with the AMPK complex, stimulating fatty acid oxidation, glucose uptake in skeletal muscle, and suppression of de novo lipogenesis.
- **Folate cycle modulation:** MOTS-c inhibits the folate cycle and de novo purine synthesis pathway, creating a metabolic stress state that triggers adaptive AMPK activation, mimicking the beneficial effects of caloric restriction at the cellular level.
- **Nuclear translocation under stress:** In response to metabolic or oxidative stress, MOTS-c translocates to the nucleus and modulates the transcription of genes involved in antioxidant defence, glucose metabolism, and mitochondrial biogenesis.
- **Insulin sensitisation:** MOTS-c enhances insulin-stimulated glucose uptake in skeletal muscle and reduces hepatic insulin resistance by suppressing lipid accumulation and inflammatory signalling in liver tissue.
- **Exercise-mimetic effects:** Circulating MOTS-c increases in response to exercise, and exogenous administration in preclinical models replicates exercise-associated improvements in metabolic flexibility, physical performance, and body composition.
- **Anti-aging and longevity signalling:** MOTS-c levels decline with age; supplementation in aged mouse models restored metabolic fitness, reduced adiposity, and extended healthy lifespan markers, consistent with its role as a mitochondrial longevity signal.

### 3. FlexPen Operating Instructions

The VitalPep Pro FlexPen is a reusable multi-dose injection pen pre-filled with MOTS-c (20 mg / 3 ml). Each unit on the dose dial delivers exactly 0.01 ml (10 µl) of solution containing 0.0667 mg (66.7 µg) of MOTS-c. The pen accepts standard 31-gauge or 32-gauge pen needles (4–8 mm). Follow the steps below before every injection.

#### ■ Step 1 — Prepare the pen

Remove the pen cap. Inspect the cartridge window: the solution should be clear and colourless. Do not use if particulates are visible or if the solution appears cloudy or discoloured. Attach a new sterile pen needle by screwing it clockwise until firmly seated. Remove both the outer and inner needle caps and set aside.

#### ■ Step 2 — Prime the needle

Select 2 units on the dose dial by turning the dial clockwise. Point the pen needle upward and tap the cartridge gently to collect any air bubbles at the top. Press the injection button fully until it clicks and a small stream (or droplet) appears at the needle tip. Repeat if no flow is seen. Priming removes air and confirms the pen is working correctly.

#### ■ Step 3 — Set your dose

Dial your required dose by turning the dose selector clockwise. For a 2 mg dose, dial to 30 units; for a 5 mg dose, dial to 75 units. The current dose is displayed in the dose window. You can turn anti-clockwise to reduce the dose before injecting — the pen will not dispense solution while dialling.

#### ■ Step 4 — Choose the injection site

Subcutaneous injection sites: abdomen (at least 5 cm from the navel), outer thigh, or upper arm. Rotate sites with each injection to avoid lipohypertrophy. Wipe the skin with an alcohol swab and allow to air-dry for 10 seconds before injecting.

#### ■ Step 5 — Inject

Pinch a fold of skin with two fingers. Insert the needle at a 45–90° angle (use 90° for a 4 mm needle, 45° for longer needles). Press the injection button slowly and firmly until it stops. Hold the button down and count to 10 seconds before withdrawing — this ensures full dose delivery and prevents backflow.

#### ■ Step 6 — Withdraw and recap

Withdraw the needle at the same angle it was inserted. Do not rub the injection site. Replace the outer needle cap using the one-hand scoop method, then unscrew and safely dispose of the used needle in a sharps container. Replace the pen cap. Never store the pen with the needle attached.

#### ■ Step 7 — Storage after use

Store the pen at 2–8 °C (refrigerated) when not in active use. Do not freeze. The pen may be kept at room temperature (up to 25 °C) for a maximum of 28 days during an active dosing cycle. Record the date of first use on the pen label.

**■ Always use a new sterile needle for each injection. Sharing pens or needles poses a serious infection risk. The cartridge is pre-filled and sealed — do not attempt to refill or modify the pen.**

## 4. Research Dosing Protocol

**Concentration** 6.667 mg/ml — 1 unit on the pen dial = 0.01 ml = 0.0667 mg | 15 units = 1 mg | 30 units = 2 mg | 75 units = 5 mg

The following protocol reflects typical research parameters reported in published preclinical and early-phase human studies. Dosing is administered subcutaneously once daily. All protocols are for research use only.

Phase	Duration	Dose	Pen Units	Frequency	Route
Phase 1 — Introduction	Weeks 1–2	2 mg	30 units	Daily	SubQ
Phase 2 — Escalation	Weeks 3–4	5 mg	75 units	Daily	SubQ
Phase 3 — Research Peak	Weeks 5–8	10 mg	150 units	Daily	SubQ

**Pen longevity:** At the 2 mg introduction dose (30 units/day), the 20 mg cartridge provides approximately 10 daily doses. At the 5 mg escalation dose (75 units/day), the cartridge provides 4 daily doses. At the 10 mg research peak dose (150 units/day), the cartridge provides 2 daily doses.

■ **Note:** Some research protocols use 5 mg administered 5 days on / 2 days off rather than continuous daily dosing. Standard research cycle length is 4–8 weeks followed by a 4-week washout period. Adjust protocol based on specific research objectives.

## 5. Storage & Handling

<b>Unopened pen</b>	2–8 °C (36–46 °F) · refrigerated · protect from light
<b>In-use pen</b>	Up to 25 °C for a maximum of 28 days · keep away from direct sunlight
<b>Do not freeze</b>	Freezing causes irreversible peptide aggregation and loss of activity
<b>Transport</b>	Use a cool pack (2–10 °C); avoid prolonged exposure above 30 °C
<b>Expiry</b>	NL-2026-MC · 10/2028 · do not use after expiry date
<b>Disposal</b>	Dispose of used needles in a certified sharps container per local regulations

## 6. Safety, Contraindications & Adverse Effects

■ **RESEARCH USE ONLY.** MOTS-c FlexPen is not approved by any regulatory authority for human therapeutic use. This product is intended exclusively for in vitro and preclinical research by qualified investigators. It must not be used for self-administration or human therapeutic purposes.

- **Injection site reactions:** Transient erythema, mild oedema, or bruising at the subcutaneous injection site are the most commonly reported effects in animal studies.
- **Hypoglycaemia risk:** Due to insulin-sensitising activity, co-administration with insulin or other glucose-lowering agents in research models requires careful monitoring of blood glucose levels.
- **Cardiovascular monitoring:** As MOTS-c influences mitochondrial energy metabolism, comprehensive cardiovascular and metabolic monitoring is recommended in research protocols.
- **No human safety data:** Long-term human safety, pharmacokinetics, and drug interaction profiles of exogenous MOTS-c have not been fully established in controlled clinical trials.

## 7. References

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[1] Lee C, et al. MOTS-c: A mitochondrial-derived peptide regulating muscle and fat metabolism. *Cell Metabolism*. 2015;21(3):443–454.

[2] Reynolds JC, et al. MOTS-c is an exercise-induced mitochondrial-encoded regulator of age-dependent physical decline and muscle homeostasis. *Nature Communications*. 2021;12(1):470.

[3] Lu H, et al. MOTS-c peptide regulates adipose homeostasis to prevent ovariectomy-induced metabolic dysfunction. *Journal of Molecular Medicine*. 2019;97(4):473–485.

[4] Zempo H, et al. A sex-specific mitohormetic response in elderly adults. *Proceedings of the National Academy of Sciences*. 2021;118(37):e2023452118.

[5] [peptidedosages.com/mots-c/](https://peptidedosages.com/mots-c/) — Research dosing reference and protocol summaries.

[6] VitalPep Pro Pharmaceuticals B.V. · Batch NL-2026-MC · Manufactured in the Netherlands under cGMP standards · [www.vitalpeppro.nl](http://www.vitalpeppro.nl)