MOTs-C is scheduled for discussion by the Pharmacy Compounding Advisory Committee (PCAC) this July

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Interest in peptides and peptide drugs has dramatically increased in recent months. On July 23rd and 24th, the FDA intends to consult PCAC regarding the potential inclusion of various peptides, specifically BPC-157, Emideltide (DSIP), Epitalon, KPV, MOTs-C, Semax, and Thymosin Beta-4 fragment (TB-500), on the 503A bulks list. To prepare for patient questions and to increase understanding in advance of the meeting, a review of available information on safety and efficacy is essential. This blog post is the first in a series that will review available information on peptide drugs up for evaluation in July.

Mitochondrial Open Reading Frame of the 12S rRNA Type-c (commonly referred to as MOTs-C) is a mitochondrial derived peptide that plays as essential role in energy metabolism, insulin resistance, inflammatory response, and aging. Endogenous MOTs-C acts in response to stress, exercise, and aging. It triggers production of antioxidant response elements and intermediates that work to regulate energy homeostatis.1 In vitro data suggests MOTs-C interacts with a variety of pathways, including activating the JAK pathway (impact on aging), inhibiting mTOR signaling (immune and aging impact), inhibition of STAT3 (improved muscle function), activation of ERK pathway (obesity prevention), and translocation of GLUT4 (reduced insulin resistance).2,3 In response to this in vitro data, animal studies to determine actual biological impact have evaluated the impact of exogenous MOTs-C on the body.

There are currently no available studies in human patients, but studies for various indications have been initiated in mice. One exploratory study evaluated the impact of MOTs-C in male mice fed a normal diet. Mice were given 5mg/kg/day divided into two doses for four days or placebo. Even over this short period of time, reductions in body weight, food intake, and blood glucose were observed in the treatment group. In addition, the treatment group had decreased levels of circulating IL-6, TNFα

inflammatory markers, and markers associated with insulin resistance. As a follow-up, researchers tested a lower dose (0.5mg/kg/day intraperitoneally over 3 weeks) in mice fed a normal diet or a high fat diet. Mice in the normal diet group did not experience weight loss, but a significant decrease in weight was noted in mice fed a high fat diet with simultaneous MOTs-C.4

Other studies have evaluated the impact of MOTs-C on exercise tolerance. One study evaluated the impact of MOTs-C on running performance under metabolic stress. Young mice were fed a high fat diet and treated with either 5mg/kg/day or 15mg/kg/day intraperitoneal MOTs-C. Mice given the higher dose showed significantly superior running capacity 10 days following treatment, with increased insulin sensitivity being noted by the 7-day marker. Mice fed MOTs-C performed significantly better in endurance and speed as compared to those in the lower dose and control groups.6 Studies in rats have similarly found improved myocardial mechanical efficiency with MOTs-C supplementation. Rats treated with 0.5mg/kg/day intraperitoneal MOTs-C for 12 weeks were noted to have improved mechanical efficiency of the myocardium during exercise training over the placebo group.7 Data on the impact of exogenous MOTs-C on exercise tolerance in humans is not available, though, studies of endogenous MOTs-C levels have noted an 11.9 fold increase in MOTs-C levels in skeletal muscle in response to exercise, as well as increases in circulating levels of MOTs-C by 1.5 fold during exercise.5

MOTs-C is also of interest for a potential impact on longevity. One mouse trial evaluating 15mg/kg three times weekly intraperitoneally showed a modest trend towards increased median and maximum lifespan by 6.4 and 7% respectively.5 Studies on endogenous MOTs-C in humans have found that higher levels of MOTs-C are associated with improved maximal leg press scores in elderly patients, though, the relationship of MOTs-C with aging in men 18 to 81 years of age has not been found to be linear.8

Though preliminary animal data is exciting, there are no current studies in human patients. An analog of MOTs-C called CB4211 was studied in a small phase 1 trial in obese patients. Patients were treated with 25mg CB4211 subcutaneously daily for 28 days. The study was not designed or powered to look at efficacy for a specific condition, but treatment was noted to be safe.8,9 Dosing protocols or information regarding future human studies on MOTs-C or CB4211 are not currently available.

Looking for more about MOTs-C and other peptides up for evaluation in 2026 and 2027? FACTS members can check out our Peptide Review Sheet, available on www.fagronacademy.us. If you're interested in listening in on the PCAC meeting, more information can be found here: July 23-24, 2026: Meeting of the Pharmacy Compounding Advisory Committee - 07/23/2026 | FDA

Highlights:

Amino Acid Sequence:3 Met-Arg-Trp-Gln-Glu-Met-Gly-Tyr-Ile-Phe-Tyr-Pro-Arg-Lys-Leu-Arg (16 amino acids)

Potential Uses:2,3 MOTs-C is of interest for potentially improving exercise tolerance, reducing inflammation, and improving lifespan and healthspan.

Regulatory Notes:8 MOTs-C is up for evaluation for potential inclusion on the 503A Bulks List. The material is set to be evaluated July 2026. MOTs-C is currently banned by the World Anti-Doping Agency (WADA)

should understand federal and state legal and regulatory requirements before handling these substances. Consultation with experienced legal counsel is recommended.

References:

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