

# Branch Experience Station: Medical Food production for Pantothenate Kinase-Associated Neurodegeneration (PKAN)

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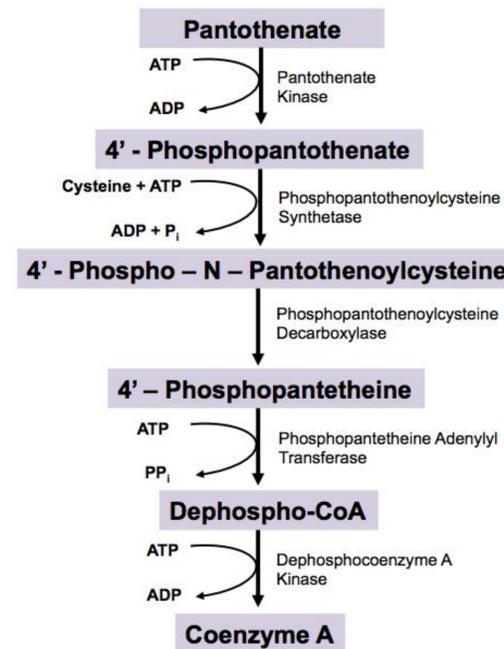
## What is a Medical Food?

This project is classified as a medical food which is defined in section "5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is "a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." Since this food is proscribed for a specific disease and passed studies have shown there is a potential for 4'-PPT to improve the lives of those with PKAN this clinical trial can be classified as a medical food.

## Coenzyme A

All patients with PKAN have a mutation on PANK2 which can be found on chromosome 20. This gene provides the information to produce an enzyme called pantothenate kinase 2. Typically this enzyme resides in mitochondria which are energy-producing centers within a cell. They help the formation of another compound called coenzyme A. Coenzyme A is essential for many different biosynthesis pathways. The effect of the deficiency of coenzyme A is not fully understood specifically how it relates to build up of iron.

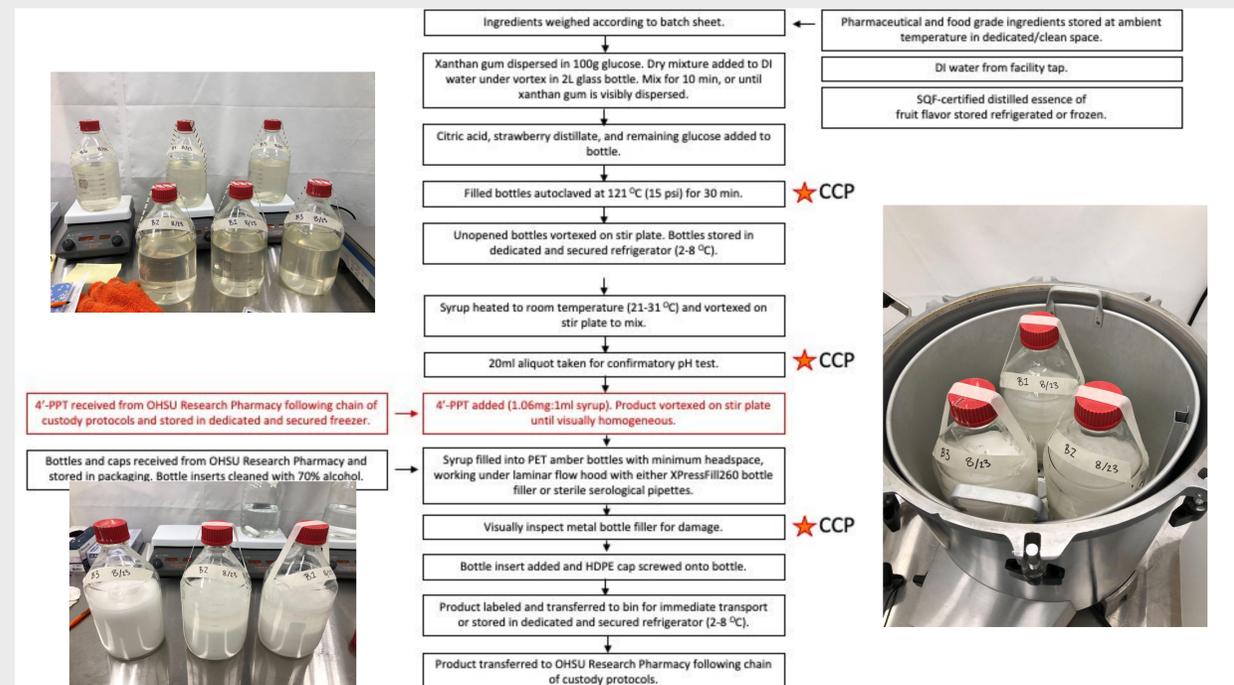
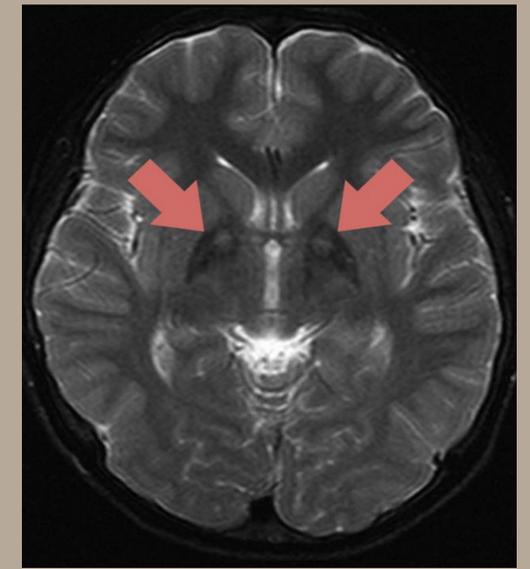
Since the recent research of PANK2 and its effect on the production of coenzyme A more work is being done on a potential treatment related to this development. This clinical trial is testing a compound, 4'-phosphopantetheine also known as CoA-Z. As described in the figure 2. CoA-Z or 4'-PPT is the product of step 3. Since patients lack the ability to make pantothenate themselves, providing one of the products in the steps could theoretically allow the body to continue the process and produce Coenzyme A within the body.



## What is PKAN

PKAN is a very rare disease and it is estimated that between 1 to 3 for every million humans are affected by this disease. Due to the rarity of this disease misdiagnosis is very common. Due to the amount of people it effect, there is a lack of funding for research. PKAN is an inherited, progressive degenerative disease and is one of the most common types of neurodegeneration with brain iron accumulation (NBIA). This specific NBIA is characterized by the degeneration of the central nervous system which results in involuntary movement of muscles and other extrapyramidal symptoms.

PKAN can be diagnosed based on symptoms, an MRI and then a molecular genetic test. Patients with PKAN will display the 'eye of the tiger' sign on a T2 MRI which is specific and unique to this kind of NBIA. The figure to the right, shows bright areas which indicate the pockets of swelling and fluid while the dark areas show iron accumulation. In most of the cases of PKAN these parts of the brain, globus pallidus and substantia nigra region are the only parts found with iron accumulation. These parts of the brain help control movement which accounts for the symptoms patients experience with this degenerative disease. Typically as the disease progresses the bright spots shrink and the darker areas increase as more iron accumulation builds over time.



Citations: Center for Food Safety and Applied Nutrition. "Guidance on Medical Foods." U.S. Food and Drug Administration, FDA, www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-frequently-asked-questions-about-medical-foods-second-edition. "MRI FINDINGS." NBIA, nbiacure.org/learn/mri-findings/. "Pantothenate Kinase-Associated Neurodegeneration." NORD (National Organization for Rare Disorders), 10 Sept. 2019, rarediseases.org/rare-diseases/pantothenate-kinase-associated-neurodegeneration/#:~:text=Affected%20Populations&text=The%20frequency%20of%20PKAN%20is,the%20accuracy%20of%20these%20estimates.

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