PREMARKET NOTIFICATION  SYNTHETICALLY PRODUCED HYDROXYCITRIC ACID

SUBMITTED BY

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1. NAME AND ADDRESS OF DISTRIBUTOR AND CURRENT MANUFACTURER

Dietary Supplement Distributor:
Broderick & Tourville
26 Washington Street
3rd Floor
Morristown
NJ 07960

Dietary Ingredient GMP Manufacturer:
Mingchen ChemPacific Ltd
741 Moganshan Road
Hangzhou
China

Dietary Supplement GMP Manufacturer/Bottler/Packager
Shannon Minerals Limited
Upper Clare Street,
Limerick,
Ireland

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2. NAME AND IDENTITY OF NEW DIETARY INGREDIENT

Chemical Name: \((2S,3S)-2\)-Hydroxycitric Acid

Other Name: \((-\)-Hydroxycitric Acid

Common Names: Hydroxycitric acid, HCA, hydroxycitrate, \((-\)-hydroxycitric acid, \((-\)
HCA, \((-\)-hydroxycitrate

(See also \(\) Hydroxycitric Acid \(\) The principal Acid in the fruits of Garcinia Cambogia Desr.,
Lewis and Neelakantan, Central Food Technological Research Institute, Mysore, India, March 1964) –
(Appendix A)

The new dietary ingredient is branded APPETRIM™
3. DESCRIPTION OF THE PRODUCT CONTAINING SYNTHETICALLY PRODUCED HCA

The dietary supplement is a 500 mL solution containing 700 mg (-)-HCA, the dietary ingredient. The dietary ingredient is provided by APPETRIM™ synthetic tripotassium hydroxycitrate.

The product is to be sold in individual bottles containing 500 mL of dietary supplement. The product ingredients are water, citric acid, APPETRIM™ synthetic tripotassium hydroxycitrate, natural flavor, aspartame, potassium sorbate and sodium benzoate as preservatives, and aspartame potassium.

The dietary supplement is to be branded TRIM™.

Conditions of use:
The label will recommend use as a dietary supplement by consuming one bottle four times daily (one hour before a meal). It will not be recommended for use by young children or by pregnant or lactating women. The label will provide the phenylketonurics cautionary statement (21 CFR §172.804(d)(2)).

Processing and method of manufacturing
Information on production of the APPETRIM™ synthetic tripotassium hydroxycitrate, the source of the HCA dietary ingredient, including quality checks, tests, and specifications to ensure its identity, is set forth on following pages. Similarly, information on the TRIM™ Dietary Supplement, including its processing and quality control and other procedures in place to ensure its safety, is set forth on following pages. Pages containing trade secret or confidential commercial information believed to be exempt from disclosure when this notification is published at the Dockets Branch are marked “CONFIDENTIAL.”
4 HISTORY OF USE / SAFETY EVIDENCE

(See also appendices A and B)

HISTORY OF USE
The following extract briefly outlines the history of use of HCA:

Garcinia Cambogia is one of several closely related Garcinia species from the plant family known as
Guttiferae. With a thin skin and deep vertical lobes, the fruit of Garcinia Cambogia is about the size of
an orange, but looks more like a small yellowish or reddish pumpkin. When the rinds are dried and
cured in preparation for storage and extraction, they are dark brown in colour. Another member of the
family Garcinia mangostana, is cultivated specifically for its fruit and is not a source of HCA. These
Garcinia species are native to Southeast Asia and are usually wild-crafted, although they are
cultivated in some areas.

HCA is primarily found in the rind of Garcinia Cambogia, where 10 to (rarely) 30% of the weight of
the dried rind is HCA. This acid occurs in nature almost entirely in the form of its lactone, which has a
chemical structure and physiologic effects, which are different from those of the free acid.

Along the West coast of Southern India, Garcinia Cambogia is known as "Goroka" or "Kattecha puli"
(souring fruit). It is employed commercially in fish curing, especially in Sri Lanka (Colombo curing)
and various species of Garcinia are used in food preparation in Thailand, Malaysia and Burma.
Garcinia Cambogia is considered to be effective in making meals "more filling". Aside from its use in
food preparation and preservation, extracts of Garcinia Cambogia are sometimes used as purgatives
in the treatment of intestinal worms and other parasites, for tumours, for dysentery and in the
treatment of bilious digestive conditions.

Cloutare, Dallas and Michael E. Rosenbaum (1994) The Diet and Health Benefits of HCA
(Hydroxycitric Acid) (New Canaan, CT: Keats Publishing Inc, 1994).

Further studies indicate that Garcinia Cambogia has a long history of use as a food

Observational Study:
'The acid rinds of the ripe fruit are eaten, and in Ceylon are dried, and eaten as a condiment in
curries.'
1873) 220

Observational Study:
'Fruits are edible, but too acidic, also pickled: rind used as a condiment. Seeds yield an edible fat... A
decoction of rind is given in rheumatism and bowel complaints.'
Publications and Information Directorate, Council of scientific and Industrial Research (1986) The

Observational Study:
'Fruit yellowish or reddish, size of an orange having six or eight deep longitudinal grooves in its fleshy
pericarp. Pulp acid is of a pleasant flavour. It is dried among the Singalese who use it in curries.'
(New York: Verlag von J. Kramer, 1968) 237

SAFETY EVIDENCE
As well as having a long history of use in food, there are a vast number of research articles outlining
the safety of HCA. The most recent article published by the Burdock Group of Florida states:
In several, placebo controlled, double-blind trials employing up to 2800mg/day HCA, no treatment-related adverse effects were reported. There is sufficient qualitative and quantitative scientific evidence, including animal and human data suggesting that intake of HCA at levels up to 2800 mg/day is safe for human consumption.

and

In summary, on the basis of scientific procedures, which include human, animal, analytical, and other scientific studies, and history of exposure and use, the consumption of HCA at dose level of 2800mg/day, is considered safe.


An in vivo study conducted in 2003 by researchers at Creighton University found that:

Feed intake was significantly reduced in HCA-SX supplemented rats, demonstrating appetite suppression. None of the groups demonstrated any changes in water intake during the 90 days of treatment. HCA-SX supplementation did not alter hepatic and testicular lipid peroxidation or DNA fragmentation. Taken together, these results indicate that HCA-SX is safe and efficacious in weight management under the conditions employed in these studies.


Another in vivo study conducted in 2002 by researchers at the same Creighton University found that:

Results indicate that the LD50 of HCA-SX is greater than 5,000 mg/kg when administered once orally via gastric intubation to fasted male and female Albino rats. No gross toxicological findings were observed under the experimental conditions. Taken together, these in vivo toxicological studies demonstrate that HCA-SX is a safe, natural supplement under the conditions it was tested.


SYNTHEtically PRODuCED HCA

The similarities between the synthetic development of citric acid and hydroxycitric acid are striking, with citric acid now being almost exclusively produced synthetically. Synthetically produced HCA gives a product that is chemically and structurally identical to the substance found in nature, although contrary to the natural product, synthetically produced HCA contains only 100% HCA. All manufacturers involved in the process are manufacturing the product to GMP standards, and this is also a requirement for any prospective manufacturers.

Since the synthetically produced product is chemically and structurally identical to its naturally occurring counterpart, and since the GMP standards for manufacture are enforced, it is fair to assume that the synthetic product will perform in exactly the same way as the naturally occurring substance.
For detailed information on basic mechanisms of action, including appetite suppression, please see Appendix C. For further information on Quality Control Methodology please see Appendix D.
5. Designated Signatory

Brendan O’Mara
Managing Director
Shannon Minerals Limited
Appendix A

Contents:

Research paper – (-)- Hydroxycitric Acid – The Principal Acid in the fruits of Garcinia Cambogia Desr. Y.S. Lewis and S. Neelakantan, Central Food Technological Research Institute, Mysore, India, March 1964