Homoeopathic Pharmacopoeia Convention
of the
United States

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11/20/03

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

Re: Docket Nos. 01P-0572, 01P-0573, and 02P-0075

Dear Sir or Madam:

These comments are submitted by the Homoeopathic Pharmacopoeia Convention of the United States ("HPCUS") in connection with certain statements made in various documents in the above-referenced dockets. The HPCUS publishes the Homoeopathic Pharmacopoeia of the United States, a document which has been published for over 100 years and which is recognized as an "official compendium" by Sections 501(b) and 502(e)(3) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 351(b) and 352(e)(3) ("FD&C Act").[1]

The above-referenced dockets all involve the marketing of a product consisting of water and nicotine and called NICOWater™. It was initially marketed as a dietary supplement. In July, 2002, the Food and Drug Administration ("FDA") determined that NICOWater was not a dietary supplement, but, instead, an unapproved new drug marketed in violation of Section 505(a) of the FD&C Act. The manufacturer, QT5, Inc., is now marketing what appears to be the same product with the claim, on its web site, that "NICOWater™ is a **homeopathic formula** developed for adult smokers who suffer from the symptoms of tobacco cravings and find themselves in situations and/or environments where smoking is prohibited or discouraged." (Emphasis added.) [2]

[1] In order the continually improve the HPUS, the HPCUS has begun to publish it on a rolling basis, rather than an entirely new edition at periodic intervals. This new service is called the Homoeopathic Pharmacopoeia Revision Service. For convenience, we refer to it as the "HPUS".

[2] http://www.nicowater.com/About%20NicoWater.htm (accessed October 30, 2003).

01P-0573

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While the HPCUS believes that it has developed, over the years, a mutually beneficial working relationship with FDA, the organization does not ordinarily take public positions on particular products. The facts of this matter, however, compel us to offer the following comments.

As has been noted by other commenters in these dockets, *see, e.g.,* the March 21, 2003 comments filed on behalf of GlaxoSmithKline Consumer Healthcare, LP, nicotine, under its Latin name, nicotinum, is the subject of an official monograph in the HPUS. As such, it is an appropriate drug for use in homeopathic medicine. Some of the petitioners cite the fact that NICOWater contains nicotine at a level which is equivalent to an allopathic dose. We believe that this point is not relevant. Sections 501(b) and 502(g) of the FD&C Act clearly contemplate that a drug can exist both as an allopathic or traditional product and as a homeopathic product.

The HPUS specifies the dilutions (drug concentrations) which, based on safety, it considers to be appropriate for use as over-the-counter (OTC) remedies . Drug concentrations above this level are considered prescription drugs.[3] The official HPUS dilution level for OTC sale of nicotinum is 6X[4].

In March, 2003, QT5 petitioned the HPCUS to revise the lowest permissible OTC potency for Nicotinum HPUS from 6X to 5X[5]. The members of the HPCUS Council on Pharmacy ("COP") carefully reviewed the data presented by QT5 and permitted representatives of the company to make a presentation at the May 4, 2003 meeting of the COP. Based on the data presented by the company, as well as other recognized pharmacology sources consulted by the COP, the COP determined that there was an inadequate margin of safety, especially for children, if Nicotinum HPUS were available OTC at a dilution of 5X. The COP accordingly recommended to the Board of the HPCUS that the requested change not be made. (A copy of the minutes of that meeting are attached.) The Board adopted that recommendation in September, 2003.

FDA's Compliance Policy Guide on homeopathy, CPG 7132.15 (400.400) , provides, in part, that "[i]f the HPUS specifies a distinction between nonprescription (over-the-counter) and prescription status of products which is based on strength (e.g., 30x) – and which is more restrictive than Section 503(b) of the Act – the more stringent criteria will apply."

It is our understanding that, notwithstanding the decision of the HPCUS, QT5 is currently marketing NICOWater as a claimed homeopathic OTC drug at the 5X dilution level. The

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[3] Drug concentrations and potencies are inverse, thus as the potency level goes up, the drug concentration decreases.

[4] A homeopathic 6X is equivalent to a concentration of 0.001 mg/ml.

[5] A homeopathic 5X is equivalent to a concentration of 0.01 mg/ml.

HPCUS strongly believes that this action amounts to a public affront not only to the HPCUS and its deliberative process, but also to the "official" status bestowed upon it by the FD&C Act. We accordingly call upon the FDA to take appropriate action promptly.

Respectfully submitted,

John A Borneman III, R.Ph.,
President,
Homoeopathic Pharmacopoeia Convention of the United States

Attachment: HPCUS Council on Pharmacy Minutes May 4 2003

[6] Some of the petitioners cite the fact that NicoWater contains a drug at a level which is equivalent to an allopathic dose. We believe that this point is not relevant to the agency's decision. Sections 501(b) and 502(g) of the FD&C Act clearly contemplate that a drug can exist both as an allopathic product and as a homeopathic product.

HPCUS

Council on Pharmacy
Box 61067, Los Angeles, CA 90061

Please reply to: jborneman@hylands.com

May 4, 2003

To: Members of Council on Pharmacy
HPCUS Board of Directors

From: J.P.Borneman

Re: **COP Meeting May 4, 2003 REPORT**

The HPCUS Council on Pharmacy met at the Harbor Court Hotel, Baltimore, Maryland on May 4, 2003, convening immediately after the HPCUS Annual Meeting.

Attendees:

Jacky Abecassis	Clark Baker	J.P. Borneman	Eric Foxman
Sabine Hockenjos-Zogg	Marianne Heger	Peter Hinderberger	Didier Maillot
Thierry Montfort	Yvan Bourgault	Andy Bormeth	Mark Phillips
Michael Quinn	Wilfried Stock	Leandra Even	Anita Zieba
Denise Blume	Joyce Frye	Ronald Boyer	Mark Land
Todd Hoover			

Guests:
Petra Augustein-Caporale (HPCUS)
Margot Murphy-Moore (HPCUS)
Thierry Boiron (Boiron)
A. Balzer (Heel)
M. Lau x(QT 5)
L. Makowa (QT 5)
H. Wilner (QT 5)
F. Cecere (QT 5)
T. Owens (QT 5)
S. Bosse (Ropes and Grey)
D. Rosen (McDermott, Will and Emery)

1. Identification of substances that should be monographed

A list of substances that could be potentially be monographed (attached) was discussed. As Michael Quinn is the primary author of the list, he will make a first pass evaluation according to economic significance of the drugs and advise the chairman of up to 5 substances recommended for monographing. COP will evaluate this short list and make a recommendation to the Board.

2. Toxicology Guidelines for New Monographs

The following changes to General Pharmacy were approved by acclamation with no nays or abstentions:

Page 22 of General Pharmacy "Official Monograph review Procedure for the Homoeopathic Pharmacopoeia of the United States" the following language should be added as #2, with the rest of the section being appropriately re-numbered:

"Homeopathic medicines are prescribed according to the individual symptom picture, specific symptoms or keynotes and/or specific therapeutic indications. The potency used depends on the specific indication or clinical application of the homeopathic medication.

In order to guarantee the safety of new homeopathic medications (i.e. those that have not been in homeopathic clinical use for a long time) in humans, data on genotoxicity, acute and chronic toxicity, reproductive toxicity and carcinogenicity according to the current International Conference on Harmonization (ICH) -Guidelines are required for each new substance to be monographed in the HPUS. The toxic and carcinogenic potential of each substance will be assessed case by case. The type and number of studies which have to be conducted depend on the toxic and carcinogenic potential (e.g. results of standard battery for genotoxicity) of the substance and the intended application of the homeopathic medication (e.g. potency, long-term use)."

An FDA review of ICH Guidelines as well as specific ICH Guidelines for Genotoxicity and Carcinogenicity were distributed at the meeting. Committee members should familiarize themselves with these documents. They can be obtained electronically from the chairman on request.

3. Hypericum warning for mother tincture

The COP is concerned about the necessity for a warning for Hypericum perf. 3X and lower. The following warning in use in France:

"Warning: risk of interaction with other medicinal products. Combining this preparation with other medicinal products may render the other medicinal products less effective; suddenly stopping taking this preparation may increase the toxicity of the other medicinal products. Ask your doctor or pharmacist for advice".

Wilfried Stock agreed to circulate the warning and appropriate potencies used in Germany. COP will evaluate toxicity data and make a decision at its next meeting.

4. Change of OTC potency for the Nicotinum monograph from 6x to 5x

A sponsored request (see letter attached) was made of COP to change the lowest OTC potency for internal use for Nicotinum, HPUS from 6X to 5X.

A presentation of data was made in advance and live to the committee by David Rosen and Marcus Laux on behalf of the sponsor.

COP deliberated for quite a long period of time on the data presented and noted that much of the data concerned accidental ingestion of cigarette by children. Noting that there is a difference between nicotine and the complex cigarette, the group agreed to evaluate what data were available on ingestion of pure nicotine.

Data were provided by the sponsor and corroborated in Goodman and Gilman that the lethal dose for an adult is approximately 60 mg/70 kg. Using body weights of 10kg and 25kg and a dose volume of 30ml, the COP calculated the following:

Lethal Dose mg/kg	Body Weight kg	Dose reqd mg	equivalent potency (g/cc) in 30 ml	equivalent potency (x)	Safety Factor 100
0.8571	10	8.571	2.8571E-	4X	6X

0.8571	25	21.429	7.1429E-04	4X	X

Noting that the safety factor was 100 from a lethal dose and not from a NOAEL (No Observed Adverse Event Level) data point. After further discussion, the COP voted as follows:

Question: Should the request be granted and the OTC potency changed from 6X to 5X:

Yea: (1) Eric Foxman (Mr. Foxman disclosed that he is a consultant to the sponsor but declined recusal)

No: (15): Abecassis, Montfort, Maillot, Land. Hoover, Boyer,Frye, Quinn, Blume, Zieba, Bormeth, Heger, Bourgault, Stock, Phillips

Abstain: (5): Hinderberger, Hockenjos-Zogg, Baker, Even (Dr. Even disclosed a former relationship with the sponsor), Borneman (as chairman)

COP recommends to the Board that no change be made. Should the sponsor have other relevant data, COP welcomes receiving and evaluating it.

5. S&C Requested action on Ephedra Vulg.

S&C submits the following for the COP meeting in May 2003:

Ephedra vulgare

Allopathic 0.5% ephedrine at 2-3 gtt q 4h is OTC. This contains 0.5mg perdose. 30 ml of the MT could contain 75.0 mg of ephedrine which is well above the 0.5 mg per dose OTC above. S&C suggests OTC 3X, HPN-Tinc.

Action: Forward to COP suggestion of Ephedra OTC 3X, HPN Tinc.

COP agrees with the request and suggests this change be made.

6. Clarification of 'finish' potencies

Member Wilfried Stock has asked the COP to consider the following:

"I like to put a question and a request to put this issue concerning the "declarational" potency and the "calculatory" potency in a homeopathic complex remedy on the agenda of COP or PRC in Baltimore.
E.g. if the OTC-list of HPCUS says Belladonna 3X, is it conform, if a homeopathic complex remedy contains this ingredient as 10 g 2X in 100 g of the mixture?
In most of the European countries this is acknowledged. In case of the HPUS I don't find such a reference. Do you think HPCUS could give such an additional recommendation in the HPRS-Abstracts 2003 page 70 under OTC? For the toxicological relevant concentration would be equivalent 3X ≙ 10 % of 2X.

In order to avoid confusion with officials I recommend to introduce such a reference especially for complex preparations in the HPRS Abstract."

COP discussed the matter and feels that General Pharmacy deals with this issue on page 68 Section 4.

7. Other Business

Eric brought to the attention of COP that a number of salts might require a change in class or alcohol strength. He will submit a list toCOP prior to the next meeting.

8. Conflict of Interest

Conflict of interest statements were collected by the chairman.

9. Database

Data bas corrections were collected and made by the chairman. Please review the updated list and suggest any corrections.

10. Next Meeting Dates:

The COP will reconvene:

By teleconference: 11/19/04 at 8:00 am PST, 11:00 am EST

Respectfully submitted,

John P. Borneman
Council on Pharmacy Chairman

Jay Borneman
Chairman, Council on Pharmacy, HPCUS

10-Nov-02

Dear Mr. Chairman,

Attached is a list of Homeopathic medicines which are not presently monographed in the HPUS which have been ordered by customers of, and supplied in one form or another by, Hahnemann Laboratories, Inc of San Rafael, California. Some of these medicines have been prepared by Hahnemann Laboratories and others have been obtained from other Homeopathic manufacturers or pharmacies either in the US or abroad. I am sure that other retailers of Homeopathic medicines could produce similar lists.

The HPCUS is looking for homeopathic medicines which should be monographed. This raises several questions. Many of these medicines have been prepared at the request of a homeopathic physician for a single prescription for a single patient. Some of these prescriptions have been based on isopathic theory, some have been based on the ideas of recently prominent lecturers, and others have been based on data and/or theories which were not disclosed. Do these medicines need to be monographed? Probably not.

Many schools of Homeopathy both here and abroad have returned to Hahnemann=s belief that participation in provings is an essential part of the development of a Homeopath. Consequently, many students have asked for assistance in the preparation of potencies for their student project, i.e. the proving of a new medicine. These student provings never meet the published standards of the HPUS for provings.

Many busy clinicians have conducted provings in the last eight years as a method of exploring the inner workings of Homeopathy and/or expanding their clinical capabilities. Most of these provings do not meet the published standards of the HPUS.

Also, certain theories promulgated by prominent clinicians and teachers claim the ability to partially or more fully predict the clinical usefulness of particular substances prior to the conduct of a proving.

Some prominent clinicians and teachers have taught that a traditional proving is unnecessary because other methods will produce faster and more significant data. These other methods are not compatible with the HPUS methods. Clinical data has been produced and utilized by these unorthodox methods.

To the disappointment of many of the clinicians behind all of the above sources of these medicines, most of these medicines are ordered only rarely by other homeopaths. None of these are commercially marketed in retail store settings. However, once prepared, the potencies exist and are not discarded in case other homeopaths may find them useful for their patients.

It can fairly be said that many of the clinicians undertaking these provings did not understand the importance of the work done by the HPCUS. Even when provided with the HPUS Guidelines they usually did not attempt to meet the standards of the Guidelines because they were simply not equipped to do so, in terms of time, effort, or funding. Additionally, many of these were prepared at a time when the HPCUS required a substantial monetary fee to review new monographs. I can safely state that the sales of all these medicines all together do

not provide the profit to pay even ~ of the fees in place several years ago. In an analysis of sales figures, it was shown that Hahnemann Labs sold about 900 different medicines in a lengthy period of time. The 450 least commonly sold medicines, taken together as a group, accounted for about 1% of total sales. Do these medicines need to be monographed?

Respectfully Submitted,
Michael Quinn, President, Hahnemann Laboratories, Inc.

REMEDY	REMEDYFN	OTHER_NAME
ALLIGAT	ALLIGATOR MISS.	ALLIGATOR, MUSCLE
AMETHYST	AMETHYST	
ANDROC	ANDROCTONOS AMURREUXI H.	SCORPION, ISRAEL
ANGEL	ANGELITE STONE	
ARA MACAO	ARA MACAO	MACAW, FEATHER
ARGEM POLY	ARGEMONE POLYANTHEMOS	CRESTED PRICKLE POPPY
ASPARTAME	ASPARTAME	EQUAL(TM) TABS
ASSISI	ASSISI ROSE	
BISON ALB	BISON BISON ALBA	BUFFALO, AMERICAN,WHITE
BOMB SYL	BOMBUS SYLVESTRIS	BEE, BUMBLE
BUTEO JR	BUTEO JAM.RAPT.	HAWK, REDTAIL(BEAK,TALON,FEATH
BUTEO JS	BUTEO JAM.SANG.	HAWK, REDTAIL (BLOOD)
CALYP ANNA	CALYPTE ANNA	HUMMINGBIRD
CANIS LUP	CANIS LUPUS TUNDRARUM	WOLF, ARCTIC
CARB BIOX	CARBONEUM BIOXYGENISATUM	CARBON DIOXIDE
CAT HAIR	CAT HAIR	CAT HAIR
CHOCO	CHOCOLATE	
COCO	COCOCOLANUM	COCA COLA CLASSIC
CORIAND	CORIANDRUM SATIVUM	CORIANDER
CORV	CORVUS COR. PRINC.	RAVEN'S BLOOD
CRT	COMPUTER TERMINAL RAYS	CATHODE RAY TUBE EMISSIONS
DANAUS PLEX	DANAUS PLEXIPPUS	BUTTERFLY,MONARCH
EPHED	EPHEDRA TRIFURCA	MORMON TEA
FALCO-P	PEREGRINE FALCON	
FAX CAEL	FAX CAELESTIS	METEORITE, ALLENDE <-SEE THIS
FD&C YELLOW	FD&C YELLOW	
FEN	FEN PHEN	

REMEDY	REMEDYFN	OTH_NAME
FUM C	FUMUS CIGARRETTI	SMOKE, CIGARETTE
GALEO	GALEOCERDO CU HEP	SHARK, LIVER
GAS SIN PLB	GASOLINUM SINE PLUMBUM	GASOLINE, UNLEADED
HAF	HAFNIUM OXIDUM	
HELIUM	HELIUM	
HELO	HELODERMA HORRIDUS	GILA MONSTER-MEXICAN-LESS TOXI
HELOD	HELODRILUS CALIG.	WORM, EARTHWORM,COMMON
HIPP AC	HIPPURIC ACID	
HIPPOCAM	HIPPOCAMPUS	SEAHORSE
HOUS DST	HOUSE DUST MITE	
HYDROG	HYDROGEN	
HYDROG PER	HYDROGEN PEROXIDATUM	HYDROGEN PEROXIDE
IASPIS R	IASPIS RUBER	RED JASPER
IGNIS	IGNIS ALC.	FIRE
INH	ISONIAZID	
JADE	JADE	JADE, GEM
JADE P	JADE PLANT	
JOHNE	JOHNEINUM	MYCOBACTERIUM PARATUBERCULOSIS
KRYPTON	KRYPTON	
LAC CAMEL	LAC CAMELINUM	CAMEL'S MILK
LAC CAN LAT	LAC CANIS LATRANS	COYOTE MILK
LAC CAN LUP	LAC CANIS LUPUS	MILK OF GREY WOLF
LAC DELPH	LAC DELPHINUM	DOLPHIN'S MILK
LAC EQ	LAC EQUINUM	HORSE'S MILK
LAC H	LAC HUMANUM	HUMAN MILK
LAC LOX AF	LAC LOXODONTA AFRICANA	ELEPHANT'S MILK (AFRICAN)
LAC LUPI	LAC LUPANINUM	WOLF'S MILK
LAC OV	LAC OVIS	SHEEP'S MILK
LAC PUMA C	LAC PUMA CONCOLOR	MOUNTAIN LION MILK
LAP MAR C	LAPIS MARMOREUS CONNEMARA	MARBLE, WHITE
LIM BRED	LIMINITIS BREDAUII	BUTTERFLY-CALIF. SISTER

REMEDY	REMEDYFN	OTHER_NAME
LINDANE	LINDANE LOTION	
LOTUS	NILUMBO NUCIFERA	LOTUS FROM INDIA
LOXOS AP	LOXOSCELES APACHE	SPIDER, BROWN RECLUSE WESTERN
LOXOS REC	LOXOSCELES RECLUSA	SPIDER, BROWN RECLUSE MIDWEST
LUNA	LUNA	MOONLIGHT
LUNAR EC	LUNAR ECLIPSE	MOON, LIGHT, ECLIPSE
LYNX CAN	LYNX CANADENSIS	LYNX
LYNX RUF	LYNX RUFUS	BOBCAT
MAIASAUR	MAIASAURA LAPIDEA	DINOSAUR BONE
MOLDAVITE	MOLDAVITUM	MOLDAVITE CRYSTALS
MOLYB	MOLYBDENUM	
MOURN DOVE	MOURNING DOVE	DOVE, MOURNING, COLUMBA PAL?)
MUSCA	MUSCA DOMESTICA	FLY, HOUSEFLY
NAU NYMPH	NAUCHELLI NYMPHACAE	LILY, RED POND (INDIA)
NEODYM I	NEODYMIUM IODATUM	
NIOB	NIOBIUM	
OLEUM LAV	OLEUM LAVANDI	LAVENDER OIL
ONCORRH	ONCORRHYNCHUS T.	SALMON, BLOOD,SPERM,EGG
ORG	ORGANIC PEANUT	
ORYZA F	ORYZA FULVA	RICE, BROWN
OVA ANSERA	OVA ANSERA	GOOSE, CANADIAN, BRANTA CANAD.
OWL FTHR	OWL FEATHER	
OXYGEN	OXYGENIUM	
OZONE	OZONE	
PAC MADR	PACIFIC MADRONE	MADRONE, PACIFIC
PELEC OCC	PELECANUS OCCIDENTALIS	PELICAN, BROWN, FEATHER
PENN A	PENNA ANSERIS	GOOSE, FEATHER
PENNA CYG	PENNA CYGNEA	SWAN, MUTE,FEATHER
PHALEA T	PHALEANOPSIS TAISUCO	ORCHID
PIX VIA	PIX VIA	ASPHALT, FROM STREET
PLAQUENIL	PLAQUENIL	

REMEDY	REMEDYFN	O...ER_NAME
POLYST	POLYSTYRENE	PLASTIC
PRASEOD S	PRASEODYMINUM SULPHURICUM	
PROZ	PROZAC	
PSEUDO	PSEUDOTSUGA MENZEZII	DOUGLAS FIR
RAINBOW	RAINBOW (SPECTRUM)	SPECTRUM
RATTUS RAT	RATTUS RATTUS	
REIN HORN	REINDEER HORN	
RHEN	RHENIUM METALLICUM	
ROSA G	ROSA GALLICA	
RUBID C	RUBIDIUM CHLORIDE	
RUBY	RUBY	JEWEL DUST
RUTHEN	RUTHENIUM	
SANG AC JUB	SANGUIS ACINONYX JUBATUS	CHEETAH BLOOD(AFRICAN)
SANG H L	SANGUIS HAL.LEUC.	EAGLE,BALD,BLOOD OR SANG AQUI
SANG PAN U	SANGUIS PANTHERA UNCIA	LEOPARD, SNOW, BLOOD
SANG SOR	SANGUIS SORICIS	RAT'S BLOOD
SANG TIGRIS	SANGUIS TIGRIS	TIGER BLOOD
SANG UR AR	SANGUIS URS ARCT(YOSEMITE)	GRIZZLY CUB BLOOD(YOSEMITE)
SANG URS AR	SANGUIS URS ARCTOS (ADAM)	GRIZZLY CUB BLOOD(ADAM)
SAPPHIRE	SAPPHIRE	SAPPHIRE
SEQ SEMP	SEQUOIA SEMPERVIRENS	REDWOOD TREE
SHASTA DA	SHASTA DAISY	
SLUG	SLUG	SLUG
SMZ-TMP	SMZ-TMP	SULPHAMETHOXAZOLE-TRIMETHOPRIM
SOL	SOL	SUNLIGHT
SOLENOP	SOLENOPSIS INVICTA	ANT, FIRE
STEEL INC	STEELUS INCORROSIVUS	STEEL,STAINLESS,#303
SULFANIL	SULFANILAMIDE	
T REX	TYRANNOSAURUS REX	
TANT	TANTALUM	
TAX BR	TAXUS BREVIFOLIA	MOUNTAIN YEW, TIP

REMEDY	REMEDYFN	OTHER_NAME
TERBUT	TERBUTALINE	
TERRAP CAR	TERRAPENE CAROLINA	TURTLE, BOX
TESTUDO	TESTUDO	TURTLE, WESTERN POND, SHELL
TETRA	TETRACYCLINE HCL	
THIMERO	THIMEROSAL	SODIUM SALT
TRILAFON	TRILAFON	PERPHENAZINE
TUNGS	TUNGSTEN	
TURQ	TURQUOISE	
VULPES V	VULPES VULPES	FOX, RED
XENON	XENON	
ZIRCON	ZIRCONIUM	

VIA EMAIL AND FEDERAL EXPRESS

March 12, 2003

Homeopathic Pharmacopoeia Convention of the United States
Attn: Clark P. Baker, Chairman of Editorial Committee
4974 Quebec Street, N.W.
Washington, DC 20016

Re: Request for a Change in the OTC Potency Level of Nicotinum from 6X to 5X

Dear Mr. Baker:

I am writing to the Homeopathic Pharmacopoeia Convention of the United States ("HPCUS") on behalf of our client, QT5, Inc., to request a change in the over-the-counter ("OTC") potency level for Nicotinum from 6X to 5X. The current HPUS monograph for Nicotinum lists the OTC potency as 6X and it really should be 5X. This request is based upon both scientific and apparent homeopathic use evidence that Nicotinum at a 5X potency level is safe and effective for OTC use.

My client is proposing to bring to market a Nicotinum 5X liquid. The total amount of nicotine contained in the final product would be approximately 4 mg, based upon the company's manufacturing and packaging methods. This amount is no more than that contained in a single piece of nicotine-containing gum or lozenge product which are currently marketed for OTC sale.

I. The Scientific Literature Supports the Proposed Change

Attached for your review as Attachment A is a report from an independent pharmacologist/toxicologist (Dr. Sandra Morseth of Milestone Biomedical, Inc.) who reviewed the available literature and whose conclusion supports this request for potency change. As nicotine-containing gums and lozenges are already available on an OTC basis, the toxicologist focused on a number of issues: attractiveness of a nicotine containing liquid; reports from poison control centers on nicotine ingestion; and factors that influence absorption.

A review of the report indicates that that Dr. Morseth used the most conservative estimates in order to assess the worst case scenarios. Specifically, her analysis of safety is based on the theoretical accidental ingestion by a 25 kg child of 4 milligrams of nicotine diluted in 500 ml of liquid. As an initial matter, Dr. Morseth points out that the ingestion of the full 500 ml of liquid by a young child is unlikely. However, assuming the ingestion of such an amount, her analysis indicates that, at worst, some children would experience acute low-level toxicity from which recovery would be expected in a few hours. Dr. Morseth states that the signs and symptoms of acute low level toxicity would be neither serious or life threatening, noting that there have been reports on children exposed to much higher nicotine doses who were either asymptomatic or suffered only mild effects from the exposure. As a result, Dr. Morseth's safety report supports QT5's request that the HPUS Nicotinum monograph be revised to allow a 5X potency for OTC Nicotinum products.

II. FDA Has Approved the Sale of Orally Ingested OTC Allopathic Drugs That Contain the Same Level of Nicotine as a 5X Nicotinum Homeopathic Product

Dr. Morseth's report further concluded that accidental exposure to 4 milligrams of nicotine in a 500 ml liquid form would be no greater than the risks associated with other currently marketed OTC nicotine products such as gums. As the HPCUS knows, the Food and Drug Administration ("FDA") has approved a number of OTC smoking cessation drug products in gum and lozenge form that contain anywhere from 2 to 4 milligrams of nicotine per dosage unit. We attach product labeling for several allopathic smoking cessation gum products as Attachment B. It is clear that FDA believes that the ingestion of 2 to 4 milligrams of nicotine an hour is safe when used according to the labeled instructions.

Based on FDA's conclusions as to allopathic nicotine-containing gum products, a homeopathic Nicotinum 5X product labeled in accord with FDA's Compliance Policy Guide 7132.15 would have a safety record equivalent to the FDA-approved nicotine products. For the HPCUS' information, QT5 intends to include in the labeling language such as the following: "Not for sale for those under 18. Proof of age required. Not for sale in vending machines or any source where proof of age can not be verified." This labeling language will further minimize any accidental risk of ingestion by children and infants by restricting the availability of the product.

III. Nicotinum at the 4X Strength Appears to be Available for OTC Use Outside of the United States

Finally, we understand from our European colleagues that Nicotinum at the 4X strength is allowable for OTC sale in both France and Germany. Attachment C contains relevant pages from the 1995 edition of a German publication, *Homoopathische Arzneimittel*, which references the use of Nicotinum at the 4D strength. It is our understanding that 4D and 4X represent the same strength. It is our further understanding that *Homoopathische Arzneimittel* is an industry publication that contains information on nonprescription drugs.

After you and your committee have reviewed this information, Both QT5 and I are sure that the HPCUS will feel confident that a 5X OTC potency level provides adequate safety protection for the public.

On behalf of my client, I want to thank you for your consideration of this request. If you have any questions, need any additional information or want to further discuss this matter, please contact me at (202) 756-8075.

Sincerely yours,

David L. Rosen, R.Ph., J.D.

cc: John A. Borneman, III, President
590 Richards Road
Wayne, Pennsylvania 19087

Eric L. Foxman, Chairman of HPCUS PRC
3741 Mitford Lane
Clinton, WA 98236

Mr. Steven Reder
President
QT5, Inc.

HOMOEOPATHIC PHARMACOPOEIA CONVENTION OF THE UNITED STATES

Conflict of Interest Statement

I, _____, as a Member of the Homœopathic Pharmacopœia Convention of the United States (HPCUS), understand the HPCUS requirement that HPCUS be made aware of potential or actual conflicts of interest of its Members with regard to any HPCUS matter that will culminate in a Membership or Committee vote or decision. I understand that a conflict of interest occurs whenever a Member has a direct, indirect, or financial interest, or the appearance of a conflict of interest, in the outcome of any matter involving HPCUS. Among other situations, a conflict of interest can arise as a result of employment relationships, consulting arrangements, the receipt of gifts of material value, honoraria or any other funding, or the promise of such future gifts, honoraria, or other funding. A conflict of interest also occurs whenever a Member has a relationship with other parties to a matter such that the relationship might reasonably be expected to affect the judgment of the Member in the particular matter, whether in a manner adverse to HPCUS or favorable to other parties to the transaction.

In keeping with this understanding, during any Membership or Committee meeting, I will openly disclose all such potential or actual conflicts of interest in a manner that will allow the conflict to be fully reflected in the meeting minutes, and for the purpose of this meeting I am disclosing the following matters:

_____ _____

Name [Signature]

_____

Date