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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

February 13, 2004

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 53735-RR, Pool Frog Mineral Reservoir
DP Barcode: D297123

From: Tajah L. Blackburn, Ph.D., Microbiologist *[Signature]* 2/27/04
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Applicant: King Technology, Inc.
530 11th Avenue South
Hopkins, MN 55343

Formulation for Label:

<u>Active Ingredient(s)</u>	<u>%by wt</u>
Silver (ionic, from 0.5% AgCl)	0.37%
<u>Other Ingredient (s)</u>	<u>99.63%</u>
Total	100.00%

I BACKGROUND

Pool Frog Mineral Reservoir, (EPA Reg. No. 53735-RR), is a new product that uses silver chloride (AgCl) as its active ingredient. The applicant requested to register the product,

Pool Frog Mineral Reservoir, as a swimming pool water disinfectant for use in residential pools. The product must be used in conjunction with an EPA-registered source of chlorine (such as Chlorine Bac Pac). The product/chlorine system may also be supplemented with the Frog BAM Aigae Preventative (sold separately) to protect against aigae.

The applicant initially submitted laboratory data to the Agency (assigned MRID No. 454488-02); the Agency's review of this data was documented in a memorandum dated May 31, 2002. The Agency concluded that the data was acceptable, insufficient to complete product registration, yet sufficient to use a presumptive data to support an application for an Experimental Use Permit (EUP) for field trials.

The initial laboratory study compared the product-plus chlorine to chlorine alone. In addition to the need for acceptable field data, the Agency instructed the applicant to support their proposal, "that the combination of the product's silver chloride compound with free chlorine was more efficacious than chlorine alone." The Agency stated, "The silver ion has been investigated in terms of its activity against different microorganisms, however, with regard to the mechanisms of action, silver is microbiocidal only if it is in the ionic state. Since silver compounds ionize poorly, the synergistic effect needs to be explained to the Agency in more detail."

This data package contained a letter from the applicant's agent addressed to the Agency (dated September 26, 2003), EPA-form 8570-4 (Confidential Statement of Formula), two studies (MRID Nos. 461240-01 and 460835-02), Statements of No Data Confidentiality Claims for both studies, and the proposed label. The field studies (MRID No. 461240-01) were conducted by Microbac Laboratories, Inc., Venice Division, located at 115 Corporation Way Unit F, Venice, Florida 34292. The review and discussion of literature (MRID No. 460835-02) was prepared at King Technology, Inc., located at 530 11th Avenue South, Hopkins, MN 55343.

Note: During the process of reviewing the EUP, the Agency stated in correspondence (Summary of Meeting held on 9/13/01, "Frog Mineral Reservoir" Experimental Use Permit), that "[t]here are no currently registered products that contain silver chloride as the active ingredient. Therefore, any application for registration involving silver chloride will be treated as a new chemical submission."

Note: EPA Form 8570-4 (Confidential Statement of Formula) contains Confidential Business Information. Data or information claimed by the applicant to be FIFRA confidential has not been included in this report.

II USE DIRECTIONS

The product is designed to be used for disinfecting swimming pool water in residential swimming pools. Directions on the proposed label provided the following information regarding preparation and use of the product as a swimming pool water disinfectant: Before using the product for pool maintenance, balance the pH of the pool water to between 7.2 and 7.8 and total alkalinity between 60-120. Shock the pool with a chlorine shock per the manufacturer's directions. For cartridge systems, use the product inside the Frog Cyclor. For skimmer systems, use the product inside the skimmer basket. [Use of the product in skimmer systems

is limited to in-ground pools.] Use the product with 0.25-1.0 ppm of an EPA-registered source of chlorine. Use one Pool Frog Mineral Reservoir for 6 months or one season, whichever is shorter.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Disinfectants for Waters in Swimming Pools, Spas, Hot Tubs, Whirlpools, and Jacuzzis – Confirmatory Field Testing

Swimming pool (and spa) water disinfection presents a unique combination of variables, including the number of swimmers/bathers, the frequency of use, the frequency with which the water is changed, general environmental conditions, and the type/degree of organic contamination of the water by the swimmers/bathers (e.g., suntan lotions and oils) and by various debris. As a result, both laboratory testing and confirmatory field testing are required.

Confirmatory field testing must take place in at least two swimming pools (or spas), under an Experimental Use Permit, lasting for an entire swimming season (4 to 12 months). Reports must include at least the following data regarding the test pools:

- (i) The design of the pool, the recirculation and filter systems, and the water capacity
- (ii) The daily bather load
- (iii) The amount and identification of all chemicals added daily (specifying time, site and method)
- (iv) The range of chemical characteristics of the water, such as pH, nitrogenous substances, metals and hardness
- (v) The physical characteristics of the water, including temperature and clarity, determined at least daily
- (vi) Daily meteorological data, including air temperature, rainfall, and number of hours of sunlight for outdoor pools
- (vii) Bacteriological monitoring should be conducted daily, in accordance with the suggested Ordinance and Regulations Covering Public Swimming Pools of the American Public Health Association. Water samples for bacteriological analysis should be taken on opposite sides of the pool in the shallow area and as remote as possible from the inlets, preferably at the midpoints between inlets. A minimum of 144 samples should be taken during the test period. Samples should be taken just below the surface of the water, and preferably at such times when the number of persons using the pool during the preceding hour has been at least 50% of the maximum bather load of the pool, and the number of persons in the pool water at the time the samples are collected is at least equal to 25% of the maximum bather load of the pool. Pertinent chemical characteristics of the pool water at the sampling site should be determined at the time of sampling.
- (viii) The concentration of the antimicrobial agent in the water monitored daily at the same time-intervals that the bacteriological assay samples are obtained
- (ix) The method that the product user will employ for monitoring the level (ppm) of antimicrobial agent in the water.

Field test results must show that 85% of the samples collected meet the following indices (i.e., or that not more than 15% of the samples collected fail the following indices): (1) The standard plate count at 35°C shall not exceed 200 colonies/1.0 mL; (2) The most probable

number of coliform bacteria shall be less than 2.2 organisms/100.0 mL. When the membrane filter test is used, there shall be no more than 1.0 coliform organisms/50 mL; and (3) The most probable number of enterococcal organisms shall be less than 2.2 organisms/100.0 mL. When the membrane filter test is used, there shall be no more than 1.0 enterococcal organisms/50 mL. These Agency standards are presented in DIS/TSS-12.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 461240-01 "Frog Mineral Reservoir – 2002 Field In-Use Test," by J.E. Hill, David J. Brookman, and Nicole A Weulander. Study conducted by Microbac Laboratories, Inc. Study completion date – August 18, 2003.

This study documented a field test run for 7 months. The field test was conducted using two residential swimming pools equipped with water filters and re-circulation systems. Pool No. 1 contained 8,000 gallons of water when filled, and was in-ground, equipped with a cartridge filter, and enclosed in a screened porch. Pool No. 2 contained 12,000 gallons when filled, and was above-ground, equipped with a sand filter, and located in a clearing. One lot of the product, Pool Frog Mineral Reservoir (Lot No. 1068), was used during the field test. The product was placed inside a Frog Cycler, that was plumbed into the recirculation system of each swimming pool. Chlorine was added to the pools as needed, based on results from on-site estimates made with commercial test kits of the type used by the homeowners (specifically, Basic 4 Pool Test Kit). Two sources of available chlorine were used, namely an aqueous solution containing 10.5% sodium hypochlorite (Aquaguard Chlorinating Solution, EPA Reg. No. 033-458-20002) and trichloroisocyanuric acid tablets (Pool Frog Bac Pac, EPA Reg. No. 53735-2). The second source was used in both swimming pools during the summer month to provide stabilized chlorine levels.

Sampling was performed in both pools at the stairs (ladders) and the skimmers. Samples were taken approximately 5-6 inches below the water surface using polycarbonate bottles to collect water for chemical analyses and Whirpac Thio Bags to collect samples for microbiological analyses. Samples for silver, iron, and copper analyses were preserved with nitric acid. All analyses were performed as soon as possible; microbiological samples were given a maximum 2-hour hold time.

Note: The distance between sampling locations (i.e. stairs and pool inlet) were not identified.

The following parameters were tested daily (i.e., at least five times per week (most weeks)): free available chlorine (via EPA Method 330.4), silver ions (via atomic absorption spectrometry), pH, air temperature, water temperature, clarity/turbidity (via EPA Method 180.1), bather load, heterotrophic bacteria (by Standard Methods 9215D), *Enterococcus* species (by Standard Methods 9230C), *Pseudomonas aeruginosa* (by Standard Methods 9213E), and fecal coliform bacteria (*Escherichia coli*) (by Standard Methods 9222D).

The following parameters were tested monthly: iron (via atomic absorption spectrometry), copper (via atomic absorption spectrometry), alkalinity (via EPA Method 310.1), nitrogen ammonia (via EPA Method 350.3), calcium hardness (via EPA Method 215.2), and chloride (via EPA Method 325.3).

Note: Protocol deviations/amendments reported in the study were reviewed and found to be acceptable.

Note: The applicant provided indication that certain data (by date and pool) failed for various reasons including protocol deviations, incomplete data sets (cause not specified), and no record of raw data. No actual data were provided, however, for those "failed" sampling events.

2. MRID 460835-02 "Frog Mineral Reservoir Silver and Chlorine Synergy Discussion," by John Hill, PhD. Study conducted at King Technology, Inc. Study completion date – August 18, 2003.

This literature review evaluated currently available information on how silver interferes with the normal metabolic processes of microorganisms. The goal of the study was to address how silver ions (Ag^+), in the low parts per billion (ppb) range, can exert an antimicrobial effect on waterborne pathogens, especially in the presence of low concentrations of a halide such as chlorine. The review focused on silver toxicity (uptake, accumulation/resistance, and intracellular targets), and cited 23 references.

Note: Because this study was a literature review, this analysis does not meet Good Laboratory Practice standards. The report asserts that the primary studies followed accepted scientific practice and each appeared in reputable, peer-reviewed scientific journals.

V RESULTS

A. Summary of Microbiological Testing– All Water Samples

MRID Number	Parameter	As Reported by the Laboratory		As Determined by the Agency*	
		Pool 1	Pool 2	Pool 1	Pool 2
461240-01	Number of water samples examined	216†	215†	175	175
	Number of water samples exceeding DIS/TSS-12 limits	29	32†	26	28
	Percentage exceeding DIS/TSS-12 limits	13.4%	14.9%	14.8%	16.0%
	DIS/TSS-12 criterion	≤15%	≤15%	≤15%	≤15%

* The tabulated data in the laboratory report identified some samples as duplicates. The field laboratory report did not describe the procedures followed to collect duplicates as samples; therefore it is unknown whether duplicate samples represent samples taken from the same or different location of the pool. In our evaluation of the data, the Agency believes it inappropriate to "count" duplicate samples as 2 samples.

† The Agency was unable to reproduce this value reported in the summary table of the laboratory report [see Table C. Summary– Microbiological Tests in All Water Samples]. See above note.

B. Summary of Microbiological Testing– Water Samples with Free Available Chlorine Concentrations in the Range of 0.23-1.0 ppm

MRID Number	Parameter	As Reported by the Laboratory		As Determined by the Agency*	
		Pool 1	Pool 2	Pool 1	Pool 2
461240-01	Number of water samples examined	86†	72†	72	60
	Number of water samples exceeding DIS/TSS-12 limits	10	5	9	4
	Percentage exceeding DIS/TSS-12 limits	11.6%	6.9%	12.5%	6.7%
	DIS/TSS-12 criterion	≤ 15%	≤ 15%	≤ 15%	≤ 15%

* The tabulated data in the laboratory report identified some samples as duplicates. The field laboratory report did not describe the procedures followed to collect duplicates as samples; therefore it is unknown whether duplicate samples represent samples taken from the same or different location of the pool. In our evaluation of the data, the Agency believes it is inappropriate to "count" duplicate samples as 2 samples.

† The Agency was unable to reproduce this value reported in the summary table of the laboratory report [see Table C. Summary– Microbiological Tests in All Water Samples]. See above note.

VI CONCLUSIONS

1. The submitted efficacy data (MRID No. 461240-01) do not support the use of the product, Pool Frog Mineral Reservoir, as a swimming pool disinfectant when used in conjunction with free available chlorine within the concentration range of 0.23-1.0 ppm. As shown in the Results Section of this report, the Agency was unable to reproduce the values reported in the summary table of the laboratory report. These values are key to the evaluation of the data. Our review of the data – as reported by the laboratory and based on our evaluation – indicated the following:

- When considering only water samples with free available chlorine in the concentration range of 0.23-1.0 ppm, the number of failing samples met the 15% criterion identified in DIS/TSS-12 when using both the laboratory-reported summary and the Agency-generated "counts." However, the number of water samples evaluated did not meet the minimum number of 144 required in DIS/TSS-12. DIS/TSS-12 requires that a minimum of 144 samples be taken for bacteriological monitoring. Additional bacteriological testing is needed to support the label-specified range of 0.25-1.0 ppm free available chlorine. Note that water samples for bacteriological analysis were not collected daily as specified in DIS/TSS-12.
- When considering all water samples subjected to microbiological testing, the number of failing samples met the 15% criterion identified in DIS/TSS-12 when using the laboratory-reported summary. The number of failing samples did not meet the 15% criterion identified in DIS/TSS-12 when using the Agency-generated data; 16% of the Pool 2 samples exceeded the DIS/TSS-12 limits. The number of water samples was

acceptable as the number of samples evaluated exceeded the minimum number of 144 required in DIS/TSS-12. Note that water samples for bacteriological analysis were not collected daily.

- The mean level of free available chlorine in Pool 1 samples was reported as 1.1 ppm, as compared to the label-specified rate of 1.0 ppm. However, the data indicate that free available chlorine concentrations in Pool 1 samples ranged between 0.05 - 7.75 ppm; with 37% of the water samples having greater than 1.0 ppm free available chlorine (i.e., 59 of 160 samples). The chlorine alone could be responsible for controlling the bacterial population within the pool.
- The mean level of free available chlorine in Pool 2 samples was reported as 1.1 ppm, as compared to the label-specified rate of 1.0 ppm. However, the data indicate that free available chlorine concentrations in Pool 2 samples ranged between <0.05 - 13.7 ppm; with 39% of the water samples having greater than 1.0 ppm free available chlorine (i.e., 58 of 150 samples). The chlorine alone could be responsible for controlling the bacterial population within the pool.
- When DIS/TSS-12 limits were exceeded, the number of bacteria were sometimes extremely high (e.g. 70 enterococci/50 mL found, instead of 1 or fewer per 50 mL) indicating a system in poor control.

In addition, the following information required by DIS/TSS-12 was missing from the field laboratory report:

- No times, methods, or sites of the chemical additions were documented. The dates on which chemicals were added to the pool and a description of such treatment was provided.
- Physical characteristics of the water were not determined daily. Data were not typically reported for days included in the weekend and on holidays.
- Daily information about the number of hours of sunlight for the outdoor pool was not reported.

Finally, the following list of concerns regarding the field study are documented below:

- The laboratory report indicated that data collected on several dates were rejected, however the report identified only the date, the pool affects, and the reason, but failed to include the rejected data.
- Protocol deviations were observed that were not included in the laboratory report, for an example, "daily" sample collection was defined as "at least five times per week," but samples were not typically collected on holidays, including 4-day Thanksgiving weekend, shortening the actual collection of bacteriological data to as little as a 3 days per week.

Finally, it should be noted that the field study did not demonstrate the individual effectiveness of the two agents (i.e. Ag^+ in the product versus free chlorine from any of several EPA-registered products). Therefore, the field study data has not thoroughly demonstrated the effectiveness of the product, Pool Frog Mineral Reservoir.

2. The submitted literature review (MRID No. 460835-02) was proposed to address how silver ions (Ag^+), in the low parts per billion (ppb) range, can exert an antimicrobial effect on waterborne pathogens, especially in the presence of low concentrations of a halide, as in this case chlorine. However, the submitted report was insufficient at demonstrating the synergistic effect of free chlorine and silver chloride, and subsequently the efficacy of the product, Pool Frog Mineral Reservoir. Note the following definition: Synergism: interaction of discrete agencies (as industrial firms), agents (as drugs), or conditions such that the total effect is greater than the sum of the individual effects (Merriam-Webster Online Dictionary). In the review of initial laboratory data (assigned MRID No. 454488-02), the Agency indicated that "[e]xactly how the silver ions influence the microbial activity has not been shown," thus the applicant was required to explain the synergistic effect of the silver compound with free chlorine. The Agency was seeking both efficacy information at least as much as microbial physiological information. In fact, instead of demonstrating how the silver chloride compound can freely dissociate into the toxic silver ion (Ag^+) in swimming pools, this literature review cites the work of Ghandour *et al.* (1988) in which AgCl forms in a high chloride environment, rendering the silver less toxic. Studies by Gupta *et al.* (1998) used silver nitrate and silver sulfadiazine (i.e., not AgCl) with 1–4 percent NaCl (i.e., not a swimming pool chlorine compound) as the chloride source and found that increased saline appeared to coincide with increased *E. coli* susceptibility to Ag^+ . However, Dr. Hill, the author of this literature review, did not compare the ion sources, concentrations, and solubility in the Gupta study (or other studies referenced) to the parameters achievable by using the product, Pool Frog Mineral Reservoir, and has not made the case. To demonstrate synergism, one must first demonstrate the efficacy of each agent (product) alone and then demonstrate that the combined effect exceeds the efficacy that would result from a simple additive effect.

VII RECOMMENDATIONS

1. The proposed label claims (as supported by MRID No. 461240-01) are not acceptable regarding the use of the product, Pool Frog Mineral Reservoir, as a swimming pool disinfectant with free available concentration within the label-specified range of 0.25-1.0 ppm. As noted in the Conclusions Section of this report, an insufficient number of samples were evaluated to support this specific concentration range and a number of other DIS/TSS-12 requirements were not addressed. Additionally, neither study (MRID Nos. 461240-01 and 460835-02) provided any evidence to support claims that there is a synergistic effect between free chlorine and silver ions from silver chloride.

2. The marketing claim states that the product will "seek and destroy" bacteria. Information included in the data package did not indicate that silver chloride or silver ions will actively "seek" out bacteria. The applicant must delete this claim from the proposed label.

3. The following grammatical errors should be corrected on the proposed label:

- On pages 2 and 3, change "Even if upon shaking" to read "After that time, even if upon

shaking." This suggested change will improve the clarity of information on the proposed label.

- On pages 2, 3 and 8, change "it's" to read "its." "It's" is a contraction for "it is."
- On pages 2 and 6, change "manufacturers directions" to read "manufacturer's directions."
- On page 3, change "over dosing" to read "overdosing."

4. According to the letter from the Agency, in response the Experimental Use Permit Application and Re-Submission, a deficiency regarding the proposed label was not addressed. On page 2, item #5, the recommendation is as follows:

"When submitting the revised protocol, submit a revised label which adds the following statement: After each cleaning, thoroughly drain and treat each spa tank or unit with a suitable disinfectant."

This statement, with appropriate verbiage should be included on the proposed label.