New, Slow-Dissolving DBNPA Tablets for Biocidal Treatment of Small Cooling Water Systems

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Introduction

Slow dissolving tablets of dibromonitrilopropionamide (DBNPA) are ideal for biocontrol in small cooling water systems. They are popular with water treatment service companies that treat these small cooling water systems where the low value of the account necessitates extended periods between service visits. One 200 gram tablet per 500 gallons of water is placed in an area of low turbulence in the sump to provide biocontrol for up to three weeks before requiring replacement. The tablets are comprised of 40% solid DBNPA active ingredient embedded in a ma trix of hydroxypropyl methylcellulose (27 %) and octadecanoic acid (2.5 %) with 30.5 % of inerts known only to the manufacturer. The DBNPA slowly leaches out of the binder materials and into the recirculating water, leaving behind an insoluble residue. The tablets are also known to swell and increase in volume upon first contact with water as the hydroxypropyl methylcellulose hydrates. This feature precludes the use of the tablets in floating and bypass feeder devices because the swollen tablets would fuse together in the feeder devices and plug the flow of water.

This paper reports on a new slow-dissolving form of DBNPA which overcomes these limitations of the 40 % DBNPA tablets. Statistically-designed mixture experiments were used to optimize a slow-dissolving tablet formulation comprising 97.5 % DBNPA and only 2.5 % of a blend of binder materials. Slow dissolution rate was achieved by zeroing in on an optimal blend of excipents in conjunction with tablet compaction pressure. In fact it was possible to vary the dissolution rate across a broad range by increasing the amount of excipients present. However, it was decided to develop a 100 g tablet with an identical dissolution rate to the traditional 40 % 200 g DBNPA tablets. These new tablets have several benefits and features including:

(1) Like the traditional 40 % DBNPA tablets, the new tablets can be placed on a platform in the cooling tower sump or suspended in the water in a net to avoid direct contact and corrosion of a galvanized metal basin.

(2) The new tablets do not swell and can be placed in a customized floating feeding device that is tethered in a low turbulence area of the sump. The feeding device is sealed so that there is no possibility that the user can get the hazardous DBNPA material on their skin and clothing.

(3) Unlike the traditional 40 % DBNPA tablets, the new tablets leave no insoluble residues in the tower sump.

(4) The tablets are of high tensile strength and resist breakage. Furthermore when the tablets are deliberately broken, they do not splinter and create excess dust.

(5) The new tablets are pending EPA-registration with more end use pattern applications than the traditional 40 % tablets including use of the tablets to treat small volumes of water such as evaporative coolers (e.g. swamp coolers), basement sumps and air conditioning pans.

Finally, the results obtained with the new tablets are reported for 2 recirculating cooling water field trials using the newly developed product.

EXPERIMENTAL METHODS

ANALYTICAL METHODS

The amount of DBNPA that dissolved from the tablet was measured using a modified DPD method. The same DPD method that is used for the determination of chlorine was used, except that for DBNPA a three minute reaction time was allowed before making the measurement in a colorimeter. Only 1 of the 2 bromine atoms in DBNPA responds to the DPD reagent. Since the molecular weight of DBNPA is 241.9, when a chlorine meter is used, the number reported on the display was multiplied by 3.4 because this is the ratio of the molecular weight of DBNPA and Cl_2.

TABLETING

All tablets were produced individually and in-house on a custom-machined, stainless steel die and punch. The cavity of the die measured 2.5", with the punch machined to be a few thousandths of an inch smaller to allow air to permeate from the tablet during the compression process. Figure 1 shows the die and punch used.

FIGURE 1 Custom-made stainless steel 2.5" punch and die set.

The combined weight of all pieces was 15.25 kg. A manual hydraulic Carver Press Model 2626, with a maximum compression pressure of 10,000 psi, was used to make all the new DBNPA tablet formulations. Figure 2 shows the Carver Press being used in a tablet making operation.

FIGURE 2 Carver Press Model 2626 being used to compact DBNPA crystals.

Before making the tablet, the punch and die were lubricated with a light dusting of microfine Teflon powder. The stainless steel base was then inserted into the die, a specific tablet formula (100 g) was poured into the cavity, and the punch was slowly lowered into the die and positioned on the surface of the formula. After being placed between the platens of the Carver Press, the punch and die were compacted to the desired pressure by cranking the handle. The pressure was then released, the stainless steel base was removed, and the punch and die were inverted and placed back in the press with a knock-out ring to extract the tablet from the die using force from the press.

DISSOLUTION TESTING

The dissolution testing apparatus was designed so that 8 tablets could be tested on a sideby- side basis. Figure 3 shows a schematic of the design, and Figure 4 and Figure 5 are photographs of the installation.

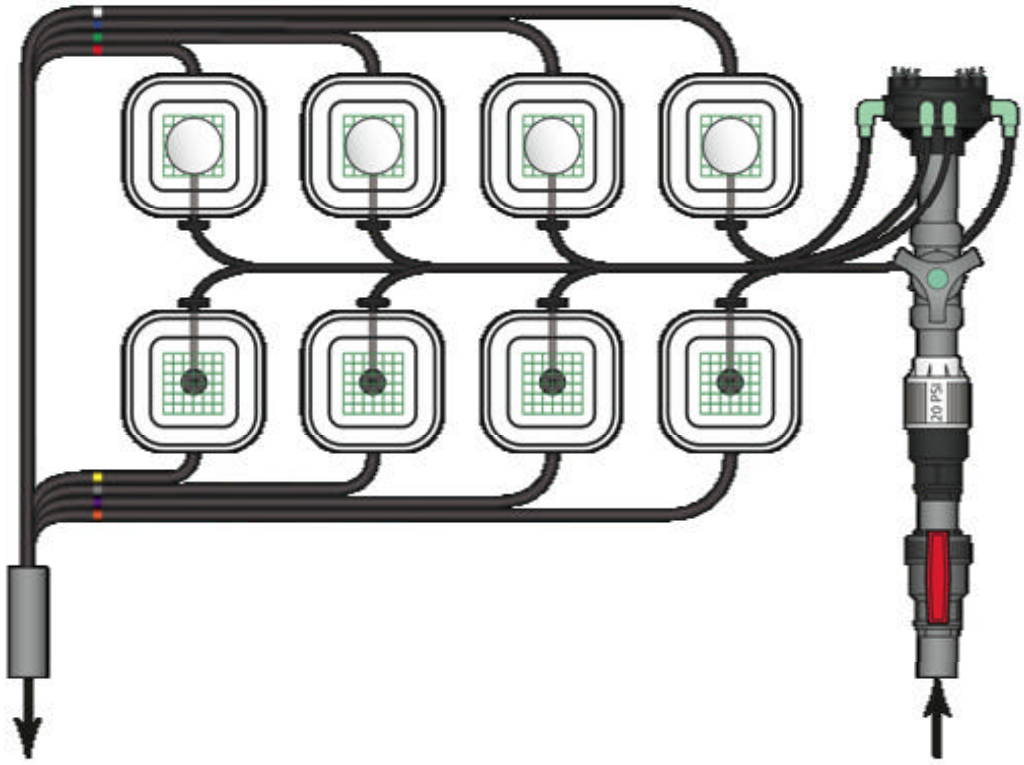

FIGURE 3 **Schematic of dissolution testing apparatus**

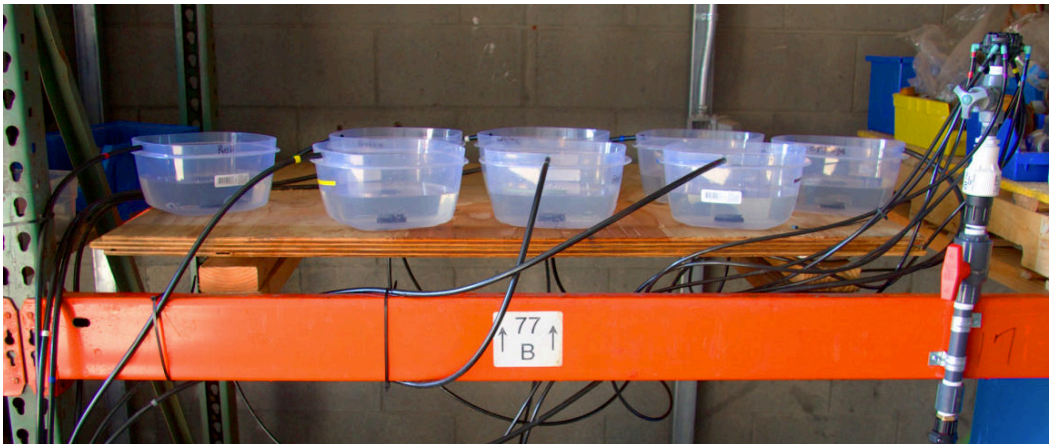

FIGURE 4 **Photograph of actual dissolution setup.**

FIGURE 5 Detail of dissolution test apparatus.

Modesto city water (with the characteristics given in Table 1) was directed through a pressure regulator to an 8-way adjustable manifold which then directed the water through inline flow regulators to provide all of the dissolution feeders with the same flowrate. The tablets were positioned in the feeders on perforated platforms so that the top and bottom of the tablets were exposed to water flow to solubilize the DBNPA.

TABLE 1 Typical properties of Modesto city water used in the dissolution tests.

pH	8.0
Calcium hardness (mg/L as CaCO3)	172
Conductivity / µScm-1	575
Total dissolved solids / mg/L	329
Total Chlorine / mg/L	0.7

Dissolution rate was gauged by measuring the amount of DBNPA in the aqueous phase over time, and since DBNPA hydrolyzes fairly rapidly in alkaline solutions such as Modesto city water, the equilibrium level of DBNPA present in the water at any time was assumed to correlate with the rate of dissolution of the tablet. As a check on this assumption, tablets were removed from the dissolution chambers after the one week test period, oven-dried, and then weighed to determine percent loss. To within ± 5 %, this percent loss gave the same value as that obtained from combining the instantaneous DBNPA residuals over time with the instantaneous flowrate of the feeders over time and integrating over the duration of the study. As a result of this correlation, the results of the study will describe the dissolution rate of the tablet in terms of the equilibrium concentration of DBNPA achieved. Additionally, this correlation served to validate the DPD test method used.

RESULTS AND DISCUSSION

OPTIMIZATION OF TABLET FORMULA

At the outset, it was decided to develop a slow-dissolving DBNPA tablet formula which dissolved at the same slow rate as the competitor product. Additional goals were:

(1) Develop a tablet with a higher level of DBNPA than the 40 % in the competitor product.

(2) Develop a tablet which can be used in a chemical feed system. This meant designing an excipient package that did not swell when hydrated in water.

(3) Develop the tablet to be used in a delivery system that eliminated the possibility of the end user contacting the DBPNA.

(4) Develop a tablet of high tensile strength that resists breakage. Furthermore when the tablet is deliberately broken, it must not splinter and create excess dust.

Statistically designed mixture experiments were used to optimize the tablet formula. This is a software-driven task available from Statease (Minneapolis, Mn) Design Expert V.8. Initially, it was hypothesized that a blend of 2 known tableting excipients might provide synergistic performance gains over the use of either alone. Thus, the variables affecting the dissolution rate were believed to be (i) Amount of excipient A;(ii) Amount of excipient B; (iii) Compaction pressure. These variables were used to populate the design and the run order was randomized to minimize the effect of nuisance variables. However, soon into the testing, it became apparent that compaction pressure had no influence on tablet dissolution rate and so the emphasis changed to focus on the other two variables. A mathematical model was fit to the equilibrium DBNPA concentration data, with the results in Figure 6.

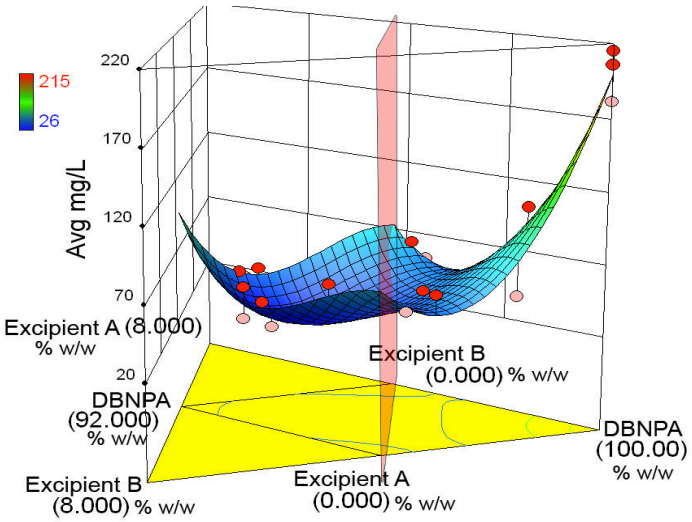

FIGURE 6 Mathematical model fit to equilibrium biocide concentration vs. composition data.

A few important conclusions can be drawn from this model:

(1) From about 0-2% total excipient, dissolution rate is strongly (and nearly linearly) dependent on excipient amount.

(2) The minimum acceptable dissolution rate appears to be around 1 % of each excipient (2 % total). Increasing the level of excipients further yielded tablets with an unacceptably low dissolution rate.

(3) A cross-section of this model at the plane indicated in Figure 6 shows the synergistic effect of the two excipients, and this is further illustrated in Figure 7. By blending the 2 excipients with the solid DBNPA, it proved possible to achieve a lower dissolution rate than with either excipient alone, and this behavior is apparent from the curvature in the cross section with a local minimum (slowest dissolution rate) at about a 1:1 blend of the two excipients.

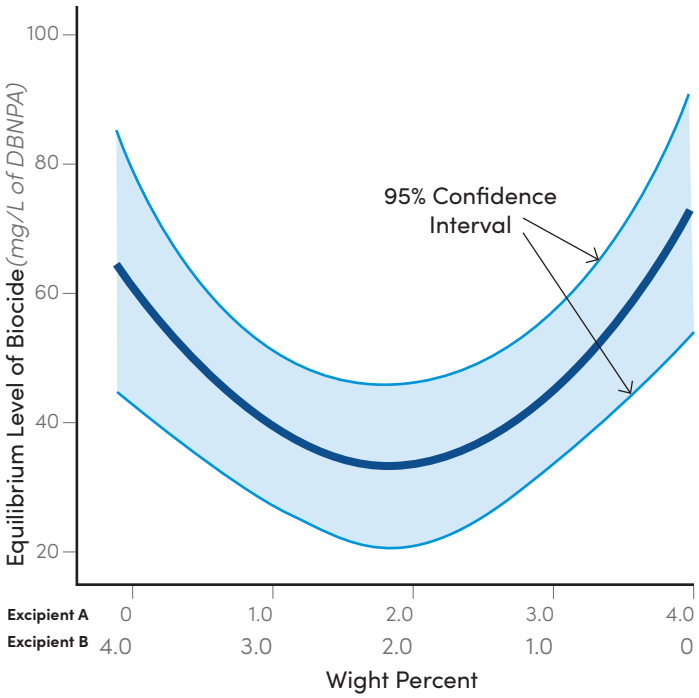

FIGURE 7 Cross-section of dissolution rate model showing synergistic effects.

Although the blend of 2 % excipient A combined with 2 % excipient B afforded the slowest dissolution rate, this tablet released DBNPA far slower than the competitive 40 % DBNPA tablet. Side-by-side comparative dissolution testing was performed using the dissolution apparatus in Figure 4. It was determined that a blend of 1.25 % excipient A and 1.25 % excipient B yielded a tablet that released DBNPA at about the same rate as the competitive product under the controlled conditions in the lab. These results are summarized in Figure 8.

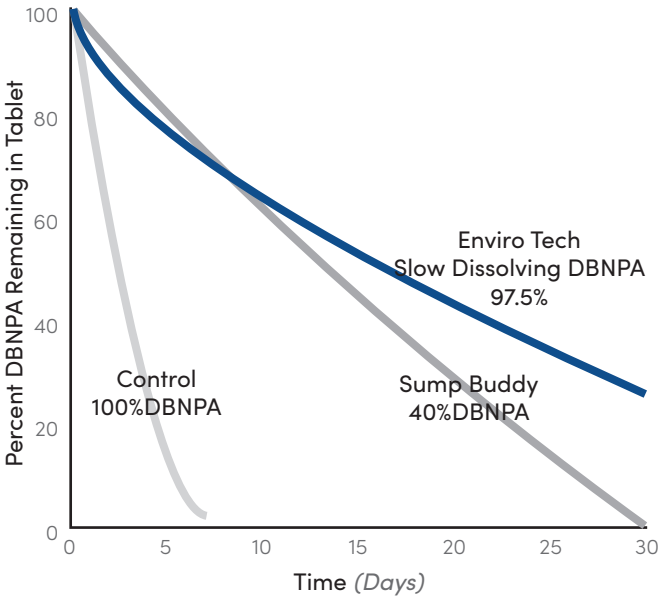

FIGURE 8 Dissolution comparison at low flowrate (1 GPH). Equilibrium concentration data has been transformed into dissolution rate data using flowrate information.

Consequently, most of the subsequent development was performed on tablets made with this blend.

TABLET STRENGTH TESTING

One important consideration when making a tablet is its structural integrity, and a part of that is how well they can take abuse in the manufacturing and shipping process. A typical measure of tablet strength is the "flexural strength", or more generally, the "tensile strength". This is easily determined for brittle materials through a three-point bend test (illustrated schematically in Figure 9) as the point at which the material "yields", or in the present case, simply snaps in half.

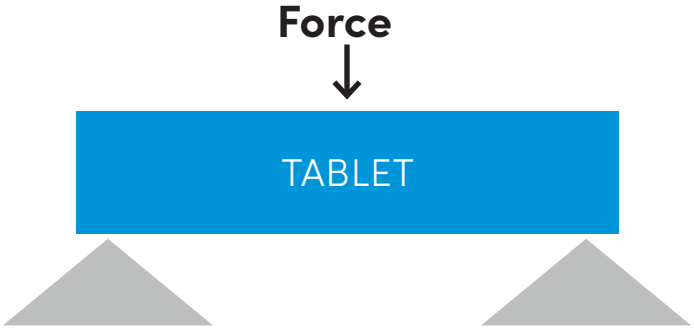

FIGURE 9 Three-point bend test used to test the fracture strength of tablets.

The criteria for a "good tablet" is one that exhibits a high tensile strength and doesn't splinter/shatter or create excess dust and powder upon fracture. Using a modified tablet hardness tester the tablet strength was determined as a function of composition (i.e. percent excipients) and compaction pressure. Tensile strength was found to be a weakly quadratic function of composition and a strongly linear function of compaction pressure, and this model is presented in Figure 10.

Figure 11 shows the exceptional fracture surface of the tablets, and Figure 12 shows how well the two halves fit back together after fracture (that is, how little material has splintered off).

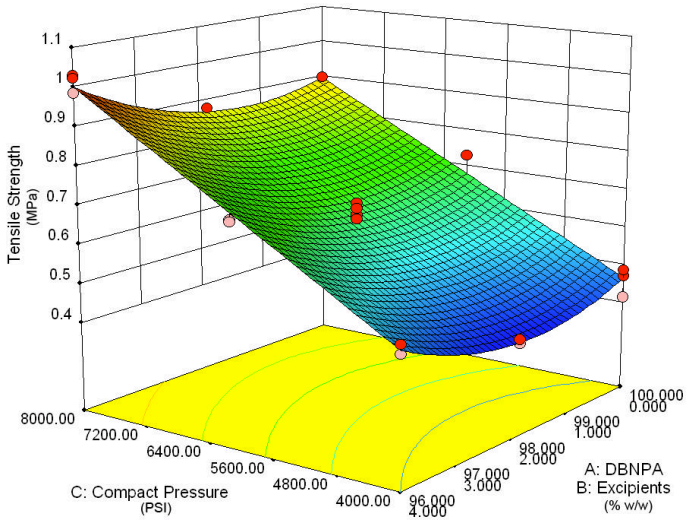

FIGURE 10 Compaction pressure and composition vs. fracture strength.

FIGURE 11 Detail showing the fracture surface of the tablets after a typical three-point bend test.

FIGURE 12 Fitting the tablet halves back together after the test shows how little material was lost as powder or splintering during the break.

FIELD TRIALS

Since the delivery method was to be a pool floater, several standard pool floaters (HTH Pop-Up Pool Floater) were tared and filled with six 100g, 2.5 inch diameter DBNPA tablets for Trial 1 (TSCV 4000 gallons) (Figure 13 and 1 tablet in the Floater for Trial 2 (TSCV 400 gallons. The floaters were adjusted for minimal flow (i.e. only one available slot in the floater exposed the DBNPA tablets to the cooling water).

FIGURE 13 Floater used in field trials.

Two field sites were selected for trials, and relevant tower characteristics were gathered for each. Floaters were weighed and positioned in their respective tower basins. Data was gathered and measurements taken at each of the thrice-weekly visits. This included:

(1) DBNPA residual present in the cooling water, both in the basin and from the recirculating water sample port.

(2) Weight of the floater so that the amount of DBNPA remaining could be gauged.

(3) Aerobic bacteria count in the tower water.

As mentioned previously, DBNPA degrades rapidly under alkaline conditions, so all measurements of the DBNPA concentration in the water were taken at the field site immediately after sampling. Additionally, sampling from different locations in the cooling tower system ensured that a representative average sample was obtained.

Trial 1. The water chemistries and cooling tower characteristics for the first trial are presented in Table 2 & Table 3. The makeup water in this tower was softened using an ion-exchange resin that was regenerated with sodium chloride as necessary.

TABLE 2 Water Chemistry for Trial 1

	pH	Cond. *(mS/cm)*	Calcium Hardness *(ppm as $CaCo_3$)*
Makeup	7.67	1.21	0
Recirculated Water	9.18	3.70	30

TABLE 3 Tower Characteristic for Trial 1

TSCV *(gal)*	ΔT *(°F)*	Cycles *(based on s)*	Prev. Biocide Program	Aerobic (init.) *(Log10 CFU/mL)*	No of Tablets in Floater
4400	15	3.06	BCDMH	2.89	6

Trial 2. The water chemistries and cooling tower characteristics for the first trial are presented in Table 4 and Table 5.

TABLE 4 Water Chemistry for Trial 2

	pH	Cond. *(mS/cm)*	Calcium Hardness *(ppm as $CaCo_3$)*
Makeup	7.82	0.318	130
Recirculated Water	9.16	1.004	380

TABLE 3 Tower Characteristic for Trial 2

TSCV *(gal)*	ΔT *(°F)*	Cycles *(based on s)*	Prev. Biocide Program	Aerobic (init.) *(Log10 CFU/mL)*	No of Tablets in Floater
400	10	3.16	N/A	2.48	1

Field Trial Results.

In total, two formulations were tested in each tower basin. Tablet weight remaining versus time is plotted in Figure 14 for all tests. Detailed trial results are presented in Table 6 and Table 7.

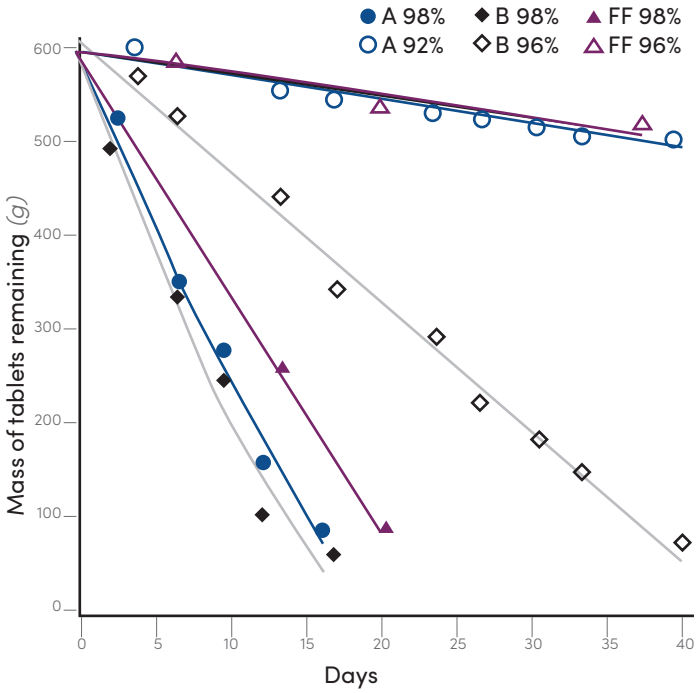

FIGURE 14 Field trial results. A: Trial 1, Basin 1 B: Trial 1, Basin 2 FF: Trial 2.

TABLE 6 Detailed results for Trial 1. Note that since the basins are joined, there is only one aerobic count for both basins. The lifespan for the 92 % formulation (4 % Excipient A and 4 % Excipent B) is an extrapolated estimation.

	Avg Residual *(ppm as DBNPA)*	Avg. Aerobic Count *(log_{10} CFU/mL)*	Lifespan *(days)*
A 98%	0.27	3.12 (± 0.17)	19
B 98%	0.27	3.12 (± 0.17)	20
A 96%	0.27	2.95 (± 0.12)	45
B 92%	0.20	2.95 (± 0.12)	~270

TABLE 7 Detailed results for Trial 2. The lifespan for the 96 % formulation (2 % Excipient A and 2 % Excipent B) is an extrapolated estimation

	Avg Residual *(ppm as DBNPA)*	Avg. Aerobic Count *(log_{10} CFU/mL)*	Lifespan *(days)*
FF 98%	0.44	3.09 (± 0.35)	23
FF 96%	0.17	3.20 (± 0.30)	~265

The 96 % DBNPA lasted far longer in Trial 2 than it did in Trial 1, and this was attributed to the lower recirculation volume, and consequently lower recirculation rate, in Trial 2.

Field Trial Conclusions

The results of these field trials confirm the laboratory findings. Namely:

- Use of 4 % excipient A and 4 % excipient B (92 % DBNPA) results in a tablet with an unacceptably low dissolution rate.
- A tablet containing between 98 % and 96 % DBNPA with the rest a 1:1 blend of excipients A and B provide a product with the targeted dissolution rate.
- The three-week replacement rate is achievable with a slight adjustment of excipient level in the tablets (97.5% DBNPA with 1.25 % excipient A and 1.25 % excipient B). This is the formulation for which EPA registration is pending.
- The preferred tablet formulations released sufficient DBNPA to maintain excellent microbiological control of the cooling water. In both trials, aerobic plate count bacteria in the cooling water were maintained below 4 log10 CFU/mL.
- Slow dissolving, 100 g DBNPA tablets of high tensile strength have been developed so that one tablet is used for every 500-1000 gallons of recirculating water requiring treatment. The new tablets have a comparable dissolution rate to a commercially-available 200 g DBNPA tablet.

Acknowledgement: Brad McGhee and James Shaw of Triton Chemical Services (a member of AWT) are thanked for identifying and making available the two cooling water trial sites.