UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

January 30, 2006

MEMORANDUM

SUBJECT: Occupational Exposure Considerations for Proposed Industrial End-Use Product ***BUSAN 1215***: New Use Pattern for the Active Ingredient **Ammonia** in Pulp and Paper Mill Process Water Systems.

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DP Barcode: D313640

Pesticide Chemical/No.: Ammonia / 005302

Registrant: Buckman Laboratories, Inc.

EPA File Symbol(s): 1448-UGE: *BCMW* (MUP for Formulator Use)
1448-UGG: *BUSAN 1215* (Industrial End-Use Product - *repack of BCMW*)

MRID No.: 464581-01

Action Requested:

The Antimicrobials Division (AD), Product Management Team 31, requested that the Risk Assessment and Science Support Branch (RASSB) conduct an occupational exposure assessment in support of the proposed industrial end-use product *BUSAN 1215* (EPA File Symbol 1448-UGG) containing 7.59% ammonia (total) as the active ingredient. Ammonia is currently registered as an active ingredient at 0.2% in only one product, AANKILL 44 (EPA Reg. No. 63709-1), an insecticide against fire ants. Therefore, the proposed industrial use of *BUSAN 1215* to control algal, bacterial and fungal deposits in pulp/paper mill process water systems constitutes a "new use" for the active ingredient.

An exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators, etc.) during use or to persons entering treated sites after application is complete. For *BUSAN 1215*, toxicological hazard has been identified for ammonia concentrates as acute dermal corrosivity and irritation to the respiratory system. Protecting occupational workers against dermal/eye injury and respiratory tract/mucosal damage from off-gassing of ammonia vapor (due to its high vapor pressure) is of particular concern for workplace safety. However, the exposure criterion is not met since proposed use conditions [closed-system delivery, personal protective equipment (PPE), industrial safety guidelines for monitoring of airborne ammonia] will negate any contact with ammonia in the workplace. Therefore, only a "qualitative" assessment is presented to address potential occupational (handler and postapplication) exposures from use of *BUSAN 1215* in industrial pulp and paper mill process water systems used in manufacturing food-contact pulp/paper and paperboard.

Review Outcome:

Based upon review of the submitted data for proposed registration of *BUSAN 1215* microbicide, AD/RASSB anticipates that the product will pose limited dermal/inhalation exposure concern for paper mill workers when handled and applied under conditions of use stipulated on the draft labeling and in Buckman's report (MRID 464581-01) detailing intended product use methods/worker activities, including exposure mitigation measures such as PPE and engineering controls, and industrial workplace monitoring of airborne ammonia.

The *BUSAN 1215* product formulation contains a low percentage of ammonia as a dilute aqueous solution (acute product toxicity category IV). The registrant stipulates handling of product by trained Buckman representatives only and mandatory use of dermal PPE. *(Note: PPE language should be added to product labeling precautionary statements.)* It is transported in sealed tote bins which are then attached to a closed, metering system. The product is pumped into the paper mill water system via a fixed piping and feed system (i.e., chemical feed skid). The mixing proportions for dosing the system are designed to consume a significant portion of the available ammonia. Overall, the product use conditions minimize any potential acute and chronic exposure risks for occupational handler/postapplication tasks.

As it pertains to worker exposure, this AD/RASSB review supports allowing the "new use" pattern for ammonia and identifies no obstacles for ***BCMW/BUSAN 1215*** product registration. We concur with Buckman's statements that: *"The low potential acute systemic toxicity, the restriction of the product to industrial use, protective closed-system application*

equipment and established regulatory guidelines for ammonia assure that this product can be safely used when handled according to label instructions."

Any future changes to the product use pattern and/or conditions of use will prompt AD/RASSB to reassess human exposure potential for *BUSAN 1215.*

Background:

The registrant held preliminary discussions with AD/RASSB in August and September of 2004 in preparation for submission of an acceptable registration application in January, 2005 for both a proposed manufacturing-use product (MUP) and industrial end-use product (EP) as *BCMW* and *BUSAN 1215* respectively. The EP, *BUSAN 1215* (EPA File Symbol 1448-UGG) is a direct repack of the formulator-use MUP, *BCMW* (EPA File Symbol 1448-UGE). Both products contain 7.59% aqueous ammonia (total ammonia) as a dilute ammonium solution formed from an aqueous suspension of [redacted] *BUSAN 1215* is applied in conjunction with a sodium hypochlorite source (12.5% a.i.) to form "monochloramine" in-situ, as the active component (microbicide) for treating pulp/paper mill water systems.[2, 3]

BUSAN 1215 was initially proposed for use in a variety of industrial cooling water system applications (e.g., cooling towers, recirculating cooling water systems, brewery/food pasteurizers, evaporative condensers, decorative fountains, and sewage/ wastewater systems) which have since been dropped from consideration by the registrant. Only the pulp/paper mill water system use patterns remain for exposure assessment. AD/RASSB will address separately (under DP Barcodes D313638 and D313639) any dietary concerns for potential ingestion of monochloramine residues leached from manufactured food-contact paper/paperboard.

To facilitate review, Buckman Laboratories, Inc. submitted draft labeling for *BCMW/ BUSAN 1215,* and data on product use (Series 875 GLN 875.1700 and 875.2700) and description of human activities (Series 875 GLN 875.2800) were provided in the Supplemental Report *"Mammalian Toxicology and Environmental Fate and Effects Data"* (MRID 464581-01) received January 31, 2005.

Overview of Product Use:

The registrant-submitted documents indicate the following product use profile for the proposed *BUSAN 1215* industrial end-use product.

[redacted]

[2] Numerous sodium hypochlorite (12% a.i.) source products (e.g., *BUSAN 1125C*, EPA Reg. No. 1448-20001) are currently registered with the Agency for use as microbicides in treating industrial process water systems (including paper mills). Therefore, the use of sodium hypochlorite for water system chlorination is an established use pattern, not subject to reassessment in support of the proposed registration of *BUSAN 1215.*

[3] The monochloramine generation process is consistent with certain alternate disinfection techniques used for public drinking water systems where ammonia and hypochlorite react in water for "chloramination".

INERT INGREDIENT INFORMATION IS NOT INCLUDED

Table 1. *BUSAN 1215* Use Profile

Pulp and Paper Mill Process Water Systems (Microbicide)	***BUSAN 1215:*** This product is used for the control of algal, bacterial and fungal deposits in influent water systems, and all process water systems used for the manufacture of paper and paperboard products. [a]
Formulation	Liquid Concentrate (Supplied in semi-bulk shipment of sealed "transfer" tote bins.)
Active Ingredient % (PC Code)	***Ammonia (total)*** **(7.59%)** *(aqueous ammonia)* (005302) (A dilute ammonium solution formed from an aqueous suspension of [redacted] [redacted])
Product Density	Bulk Density 9.59 lbs/gallon
Vapor Pressure	*Volatile* as 7510 mm Hg at 25 °C for aqueous ammonia.
Personal Protective Equipment (PPE)	***Per Labeling:*** Signal Word: CAUTION. Avoid breathing vapor. Avoid contact with skin, eyes, or clothing. ***Per Product Use Data:*** Trained Buckman representatives wear Dermal PPE for all handler tasks: protective eye-wear (goggles, face shield or safety glasses), impervious chemical-resistant gloves, and full body clothing (long sleeved shirt and long pants; socks and shoes) when handling. Inhalation PPE not specified since inhalation potential negated with use of engineering controls for closed metered delivery and established regulatory airborne exposure limit guidelines for ammonia. Although inhalation exposure is not anticipated due to use of engineered delivery systems (closed, metered feed) exposure values have been established for Ammonia which allow protective airborne monitoring for industrial workplace safety. **Exposure Values** a. IDLH: 300 ppm (NIOSH, 1997) b. TLV (8-hour TWA): 25 ppm (ACGIH, 1999) c. TLV STEL (15-minute TWA): 35 ppm (ACGIH, 1999) d. NIOSH REL (10-hour TWA): 25 ppm (18 mg/m3) e. NIOSH STEL (15-minute TWA): 35 ppm (27 mg/m3) f. OSHA PEL (8-hour TWA): 50 ppm (35 mg/m3) Legend : IDLH = Immediately dangerous to life and health ; NIOSH = National Institute of Occupational Safety and Health; TLV = Threshold limit value; TWA = Time-weighted average; STEL = Short-term exposure limit; ACGIH = American Conference of Governmental Industrial Hygienists; REL = Recommended exposure limit; OSHA = Occupational Safety and Health Administration; and PEL = Permissible exposure limit.

Use Application and Dosage Rates	***Per Labeling:*** *Use Application* **Pulp and Paper Mills:** This product is applied in conjunction with sodium hypochlorite (12.5%) to form monochloramine, a slower acting less aggressive oxidizing microbicide. The products are added to dilution water to achieve a minimum molar ratio of 1.5:1 of ammonia to oxidant, and this ratio is obtained by combining 0.6 fluid ounces of *BUSAN 1215* to 1 fluid ounce of sodium hypochlorite (12.5%). To ensure both handling safety and effectiveness, the monochloramine solution should be generated and fed into the treatment water systems through a proper chemical feed skid only by a trained Buckman representative. Use of this product for any other purposes or contrary to the use directions specified below is prohibited. Dosage Rates: When noticeably fouled, apply sufficient product and sodium hypochlorite to achieve a total chlorine residual of at least 1 ppm in excess of the system oxidant demand. Once control is achieved, treatment rates can be reduced to sub-demand rates from 50% to 80% of system demand. The product may be added to the system continuously or intermittently as needed to any area of the system where uniform mixing can be obtained. The frequency of feeding and the duration of the treatment will depend on the severity of the problem.
Mix/Load/Application Method	***Per Product Use Data:*** **Application system (closed, metered equipment)** The product will be handled and applied only by trained Buckman representatives via engineering controls (Buckman semi-bulk transfer and chemical handling systems). Mixer/Loader: *BUSAN 1215* is packaged as semi-bulk "transfer" tote bins which connect directly to a base tote feed container via specialized fittings (discharge valve/discharge hose). A small vent cap located on top of the transfer tote is opened to prevent vapor lock allowing for closed gravity flow transfer (loading). Operators are not exposed directly to any material via inhalation during unloading due to the location of the small vent cap and where they are standing when they open the transfer valves (vent cap is above them). The loading process takes less than 10 minutes. All personnel are required to use proper PPE when handling. Application: After loading, the tote containing the chemical hooks directly to a feed skid with the use of Kam-Lok quick fit connectors and open/close valves. Further safety measures taken to keep personnel exposure to a minimum is the addition of a containment vessel so that if a leak should occur, or some circumstance requires the totes to be moved, the small quantity of chemical left in the connection hose can be drained to the containment vessel for disposal. Use of dedicated skid-mounted chemical dosing system ensures closed delivery of both aqueous ammonia (*Busan 1215*) and sodium hypochlorite (12 % a.i.) into water systems for closed in-situ generation of monochloramine solution. Feeding of the reactant product (monochloramine) is through a double-lined, hard-pipe into the application site. (See rough schematic in Appendix A.)

Source: Registrant submitted *BUSAN 1215* draft labeling of December 21, 2004 and related product use data (MRID 464581-01) received January 31, 2005.

[a] *BUSAN 1215* is proposed for use in maintaining the integrity of paper mill process water systems. In contrast to paper mill "preservative use patterns", *BUSAN 1215* is not intended to preserve papermaking substrates, such as: pulp/broke, paper coatings, slurries, emulsions or papermaking chemicals/inks.

Toxicological Considerations:

An overview of toxicological considerations are presented below based on a toxicology review memorandum, "*Hazard Assessment for Ammonia and Monochloroamine*" by Deborah Smegal, MPH, Toxicologist (DP Barcode D313637) dated December 9, 2005. Refer to this review for complete details on hazard characterization and data citations. Certain text are excerpted below.

The primary toxicity hazard identified for ammonia concentrates is acute dermal corrosivity and irritation to the respiratory system. Protecting occupational workers against dermal/eye injury and respiratory tract/mucosal damage from off-gassing of ammonia vapor (due to its high vapor pressure) is of particular concern for workplace safety.

There is no evidence that ammonia is a carcinogen. Nor does it appear to be mutagenic. Data are unavailable for assessing developmental/reproductive effects. Studies in the scientific literature indicate potential neurological effects in humans following inhalation/dermal exposure.

Acute Toxicity of Ammonia (Technical Source Chemicals and Industrial Concentrates)

Ammonia is a corrosive substance and the main toxic effects are restricted to the sites of direct contact (i.e., skin, eyes, respiratory tract, mouth, and digestive tract). It is an upper respiratory irritant in humans. The skin is extremely sensitive to both airborne ammonia and ammonia dissolved in water. Dermal exposures to liquid ammonia or concentrated solutions and/or ammonia gas are frequently occupationally related and produce cutaneous burns, blisters, and lesions of varying degrees of severity. The topical damage caused by ammonia is probably due mainly to its reactivity and irritation properties. Its high water solubility allows it to dissolve in moisture on these surfaces, react with fatty substances, be absorbed into deeper layers, and inflict extensive damage. The severity of the damage is proportional to the concentration and duration of exposure; flushing with water immediately after contact alleviates or prevents effects (ATSDR 2004). [Source: Agency for Toxic Substances and Disease Registry (ATSDR). September 2004. Toxicological Profile for Ammonia. U.S. Dept. of Health and Human Services.]

Acute Toxicity of BUSAN 1215

In aqueous solution, ammonia exists in equilibrium with ammonium hydroxide. Ammonia solutions can cause severe eye/dermal damage due to their caustic nature. However, as noted above, the effects are dependent on the concentration of ammonia in the solution and the duration of exposure. The proposed *BUSAN 1215* product contains a dilute ammonium concentration. Based on a review of registrant-submitted data for *BCMW/BUSAN 1215*, the following low acute toxicity potential (Toxicity Category IV) was shown for the product formulation:

Table 2. Acute Product Toxicity Data on Busan 1215			
Guideline No./ Study Type	**MRID No.**	**Results**	**Toxicity Category**
870.1100 Acute oral toxicity	464351-08	LD_{50} > 5000 mg/kg	IV
870.1200 Acute dermal toxicity	464351-09	LD_{50} > 5000 mg/kg	IV
870.1300 Acute inhalation toxicity	464351-10	LC50 ≥ 2.08 mg/L (4-hr)	IV
870.2400 Acute eye irritation	464351-11	Minimally irritating (rabbit) Irritation cleared within 48 hours	IV
870.2500 Acute dermal irritation	464351-12	Slightly irritating	IV
870.2600 Skin sensitization	464351-13	Not a skin sensitizer (guinea pig)	NA

Source: March 16, 2005 Review Memoranda, I. Blackwell, Biologist, AD/PSB, DP Barcodes D313223 and D313227.

Inhalation Toxicity Endpoint Selection

Epidemiological Study Selected: Holness, D.L. et al. (1989) *Acute and chronic respiratory effects of occupational exposure to ammonia.* Am. Ind. Hyg. Assoc. J. 50(12):646-650.

Executive Summary: Holness et al. (1989) investigated production workers exposed to ammonia in a soda ash facility. All of the available 64 production workers were invited to participate and 82% agreed to be evaluated. The control group consisted of 31 other plant workers from stores and office areas of the plant without previous exposure to ammonia. The mean age of the workers was 38.9 years and duration of exposure was 12.2 years. Weight was the only statistically significant difference in demographics found after comparing height, weight, years worked, % smokers and pack-years smoked. The mean TWA ammonia exposures based on personal sampling over one work shift (average sample collection 8.4 hours) of the exposed and control groups were 9.2 ppm (6.4 mg/cu.m) and 0.3 ppm (0.21 mg/cu.m), respectively.

A questionnaire was administered to obtain information on exposure and work histories and to determine eye, skin and respiratory symptomatology (based on the American Thoracic Society [ATS] questionnaire [Ferris, 1978]). Spirometry (FVC, FEV-1, FEF50 and FEF75) was performed according to ATS criteria at the beginning and end of each work shift on the first workday of the week (day 1) and the last workday of the week (day 2). Differences in reported symptoms and lung function between groups were evaluated using the actual values and with age, height and pack-years smoked as covariates in linear regression analysis. Baseline lung function results were expressed as percent of predicted values calculated from Crapo et al. (1981) for FVC and FEV-1 and from Lapp and Hyatt (1967) for FEF50 and FEF75.

No statistical difference in the prevalence of the reporting of symptoms was evident between the exposed and control groups, although workers reported that exposure at the plant had aggravated specific symptoms including coughing, wheezing, nasal complaints, eye irritation, throat discomfort and skin problems. Based on the lack of subjective symptomatology and changes in spirometry, this study establishes a free-standing TWA NOAEL of 9.2 ppm (6.4

mg/cu.m). Adjustment for the TWA occupational scenario results in a NOAEL(HEC) of 2.3 mg/cu.m.

Table 3. Summary of Toxicological Dose and Endpoints for Ammonia [1]

Occupational Exposure Scenario	Dose Used in Risk Assessment	Target Margin of Exposure (MOE) for Occupational Exposure	Study and Toxicological Effects
Dermal (all durations)	A dermal endpoint was not selected. Labels will specify the use of gloves, full body clothing and eye protection. Closed delivery systems negate dermal contact with chemical during Mixing/Loading/Application.		
Inhalation (all durations)	8-hr TWA NOAEL= 6.4 mg/m^3 (9.2 ppm) 24-hr adjusted NOAEL (HEC) = 2.3 mg/m^3 (3.3 ppm) (Continuous Occupational Exposure) [a] Inhalation RfC = 0.1 mg/m^3 (Lifetime Daily Exposure for General Population) [b]	LOC for MOE = 30 [c] Based on UF = 10X (intra-species extrapolation) and 3X (database deficiencies)	Occupational Study (Holness et al. 1989) LOAEL= none Lack of evidence of decreased pulmonary function or changes in subjective syptomatology. See IRIS record (USEPA 2005a) for more detailed discussion. [2]

Source: Review Memorandum, "Hazard Assessment for Ammonia and Monochloroamine" by D. Smegal, MPH, Toxicologist (DP Barcode D313637) dated December 9, 2005.

[1] *TWA = time-weighted average, UF = uncertainty factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, LOC=level of concern , MOE = margin of exposure, HEC= human equivalent concentration, RfC = reference concentration.*

[2] *U.S. EPA 2005a. Integrated Risk Information System for Ammonia.* http://www.epa.gov/iris/subst/0422.htm.

[a] The NOAEL of 6.4 mg/m^3 (9.2 ppm) from an occupational study is based on an 8-hour TWA and was selected based on lack of evidence of decreased pulmonary function or changes in subjective syptomatology in the occupational study (Holness et al. 1989). This NOAEL is adjusted to account for continuous occupational exposure as a human equivalent concentration (HEC) of 2.3 mg/m^3according to the following equation:

NOAEL (HEC) = 6.4 mg/m^3 × (MVho/MVh) × 5 days/7 days

Where: MVho is the breathing volume for an 8-hour occupational exposure (10 m^3); and
MVh is the breathing volume for a 24-hour continuous exposure (20 m^3).

A NOAEL (HEC) of 2.3 mg/m^3 is extrapolated to 3.3 ppm:
(where 1 ppm = 0.707mg/m^3, so 2.3 mg/m^3 ÷ 0.707mg/m^3 = 3.3 ppm).

[b] The 24-hour adjusted NOAEL of 2.3 mg/m^3 is the basis of the Agency's inhalation reference concentration (RfC) presented on the Integrated Risk Information System (IRIS) and represents Agency consensus. Since ammonia is a respiratory irritant, the Agency believes that the irritation potential would limit exposure. The RfC represents an estimate of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious effects during a lifetime.

An inhalation RfC of 0.1 mg/m^3 is established as follows: RfC = NOAEL (HEC) ÷ UF

Where: NOAEL (HEC) = 2.3 mg/m^3 and UF = 30 (2.3 / 30 = 0.0766 rounded up to 0.1)

' An inhalation MOE of 30 is adequate for all durations. An uncertainty factor of 10 is used to allow for the protection of sensitive individuals (intra-species extrapolation). Because it is based on a human epidemiological study, no inter-species safety factor is required. A factor of 3 was used to account for several database deficiencies including the lack of chronic data, and the lack of reproductive and developmental toxicology studies.

cc: Doreen Aviado/RASSB/AD
Chemical/Circulation Files

APPENDIX A:

Description and Schematic of *BUSAN 1215* Chemical Feed Skid

Buckman Laboratories, Inc. submitted data on product use (Series 875 GLN 875.1700 and 875.2700) and description of human activities (Series 875 GLN 875.2800) for *BCMW/BUSAN 1215* as provided in the Supplemental Report *"Mammalian Toxicology and Environmental Fate and Effects Data"* (MRID 464581-01) received January 31, 2005. An excerpt on the dedicated *BUSAN 1215* feed equipment follows:

"BUSAN 1215 is an aqueous dilution of ammonium sulfate. The product is designed to be mixed with sodium hypochlorite (12% a.i. source) added through a carefully designed chemical feed skid that allows the two to mix and form monochloramine. The chemical feed skid is designed to allow the introduction of *BUSAN 1215* to a pipe where there is continuous flow through dilution water available. The additional dilution of the product is insured by sending the product and dilution water through an in-line mixer so that the hypochlorite and ammonia mixture will react to form monochloramine before being sent to its intended treatment location.

The chemical feed system has been designed to incorporate numerous safety features that include:

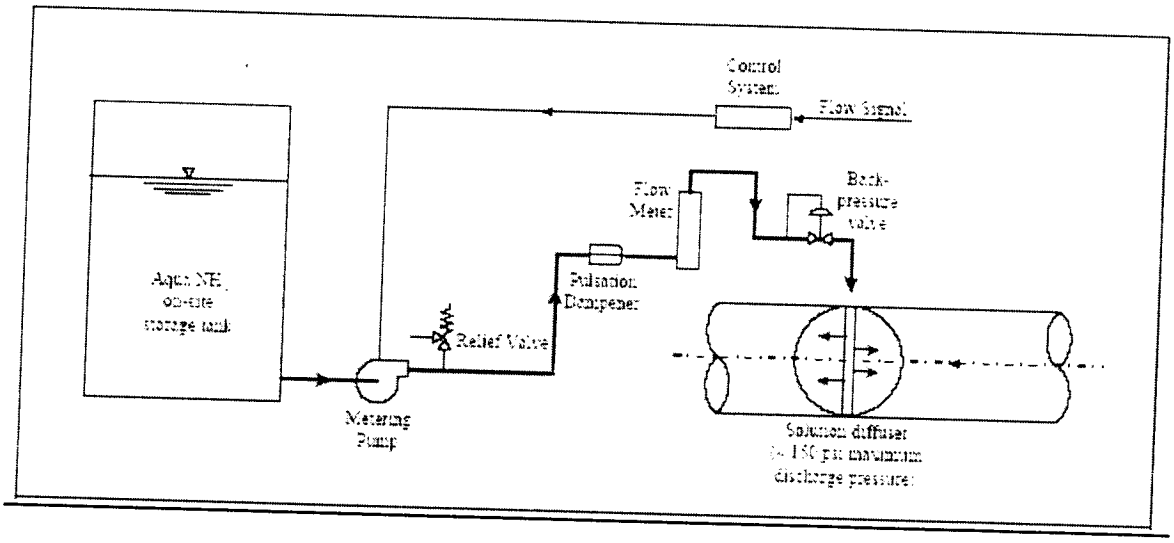
- Double walled chemical dosing lines;
- Position and size of installation connections to mother/daughter chemical tanks make it impossible to mix the chemicals external to the unit;
- Degassing lines on the outside of the unit to prevent bleach from decomposing and gassing;
- Safety shower on unit;
- Lock on unit door to prevent unauthorized entry;
- Removal of door panels on front/back to give access to all internal pumps, valves, etc..;
- Removable spill containers under all connection locks;
- Multiple shut off alarms and switches are included to prevent any unsafe condition.

For example, the following will put the unit in alarm mode:

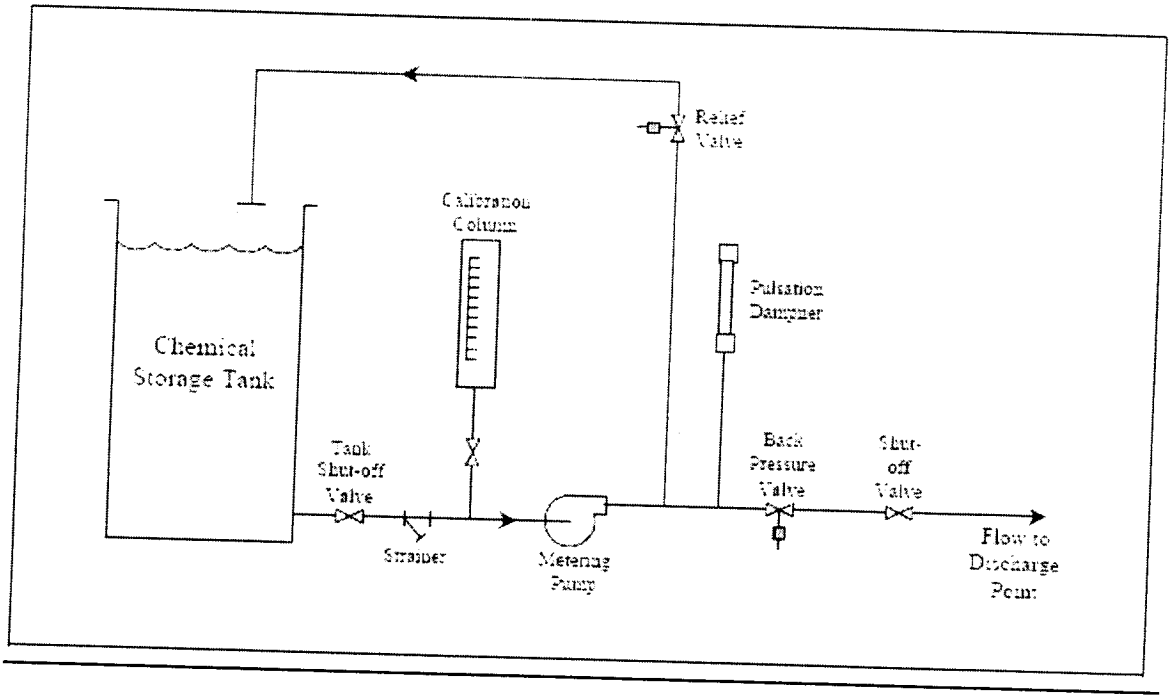
external or internal power failure,
internal leak detection sensor activated,
insufficient dilution water flow sensor,
external manual emergency shut off switch,
low chemical detection sensors.

When an alarm condition is evident, the unit stops feeding chemicals and automatically flushes all chemical feed lines with fresh water so that no storage hazards will exist. The valves that control the fresh water flush are pneumatically operated by an attached pressurized air tank so that the unit will be able to shut down safely should a power outage occur."

Generic Chemical Feed System Schematic for Water Treatment



Aqueous Ammonia Feed System



Hypochlorite Feed System

Source "Alternative Disinfectants and Oxidants Guidance Manual." US EPA, Office of Water, EPA 815-R-99-014. April 1999.

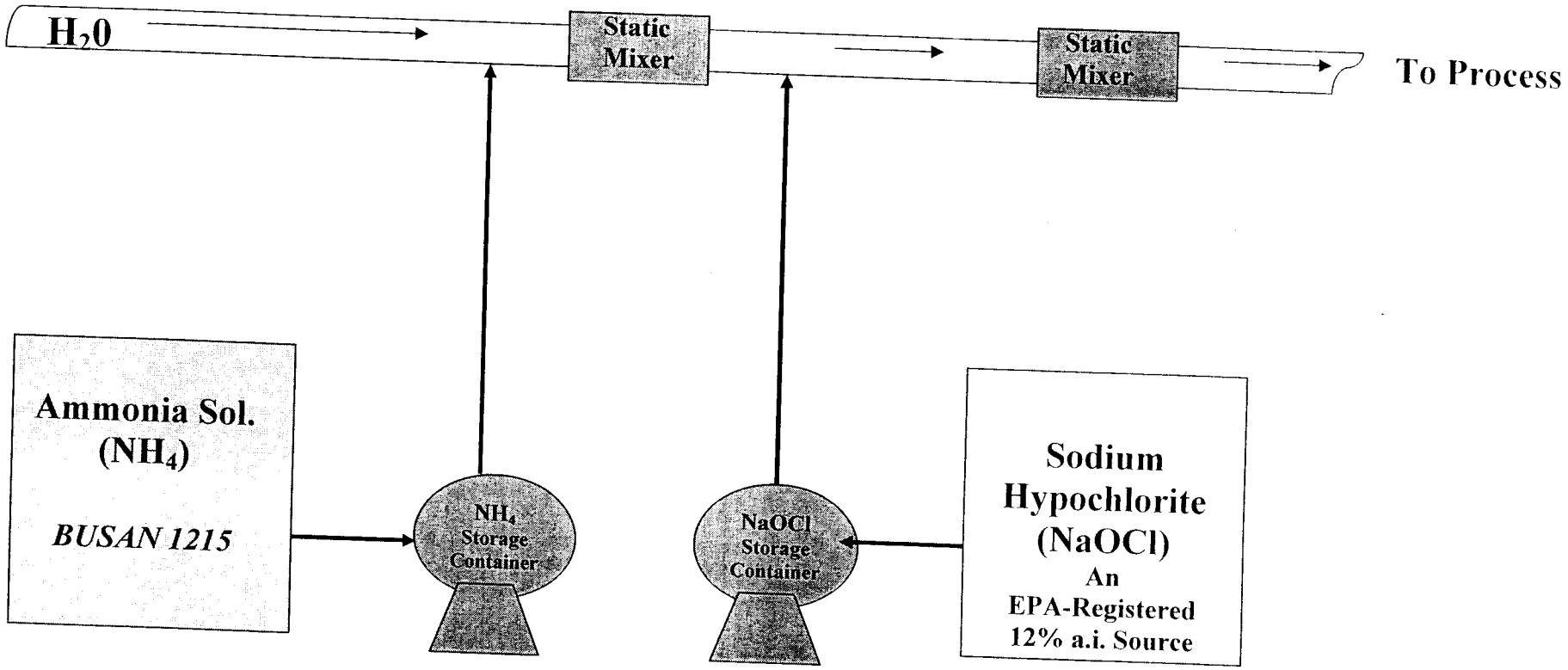


Diagram of Closed Delivery via Skid-Mounted Chemical Feed Dosing

Source: Buckman Laboratories, Inc.