REPORT

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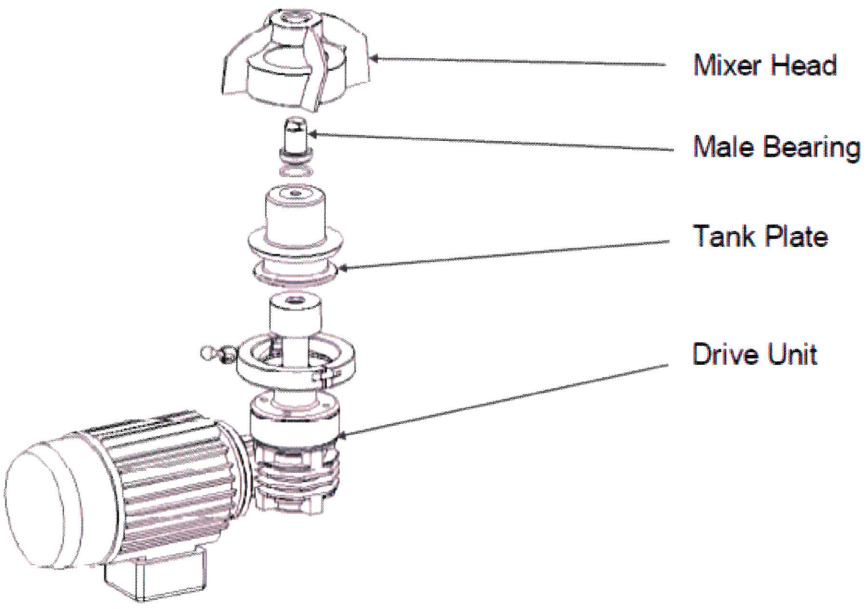
Determination of particle generation during mixing of water with KEST mixer

Assignment and objects

Determination of particles generated during mixing of water using a KEST mixer. See picture 1 below.

Table 1. *Sample information*

SP identity	Product name	Identification
6P08738:1	KEST Mixer	Steel tank approximately 200 L: No identity number. Drive unit: Motor KM-DU 20/70-1-LI ID 40681 Male bearing: ID 21110 Mixer head: ID 10828



Picture 1. Equipment tested, schematic overview from the manual sent by the commissioner.

Methods

Before starting the test, the stainless steel tank was washed > 10 times with deionized water and 6 times with Milli-Q purified water (> 18,2 M Ω, 0.22 µm filtered). Before the test was started: the tank was filled with water and a water sample was taken, filtered through a 0.8 µm cellulose acetate filter and found to contain 0 particles/ml.

The equipment consisting of a mixer head and a bearing mounted inside and at the bottom of a steel tank. The motor was mounted outside the tank and connected to a steering device, the installation was done by SP according to the instruction manual. 170 Litres of Milli-Q purified water (> 18,2 M Ω) was added to the tank and the motor started at the speed set by the steering equipment (50 Hz according to steering equipment which corresponds to 378 RPM). The top part of the tank was covered with plastic film during the mixing.

Samples of 1 litres of water was collected from the tank at specific time points. The samples were collected when the equipment was running in previously washed container and stored in a fridge before analysis. Samples were collected at 0, 0.5, 1, 12, 24 and 48 hours of mixing of the water.

Determination of particulate material

The 0.8 µm pore sized filter was weighted before filtration of the samples and was allowed to dry in a desiccator and reweight. A weight increase were calculated.

Determination of particles

The determination of > 25 and > 10 µm particles amount was done in accordance with 2013 USPC official USP <788> PARTICULATE MATTER IN INJECTIONS.

All filtration of samples were conducted in a clean room with laminar flow using equipment made of clear plastic or glass. Before filtration all equipment and filters were carefully rinsed with particle free water.

Before filtration the samples were shaken and mixed vigorously.

Samples of 0.25 to 0.5 litres were filtered through a 0.8 µm cellulose acetate filter using pressure filtration with particle free argon. Each filter was transferred to a plastic Petri dish and a lid was placed over the dish. The sizes and number of particles was determined using method *Microscopic Particle Count Test* scanning the entire surface. Three replicate determinations were done for each time point.

Determination of >5 µm and >2 µm particles were measured as amount of particles retained on a membrane filter with 5 µm or 2 µm pore size respectively (no USP method available). Samples of 0.1-0.25 litres were filtered through a 5 µm or a 2 µm cellulose acetate filter using pressure filtration with particle free argon. The filter was transferred to a plastic Petri dish and

a lid was placed over the dish. The size and number of particles were determined using method *Microscopic Particle Count Test* scanning the entire surface. Three replicate determination were done for each time point.

No visible signs of aggregation of particles was observed during the analysis of particles.

Results

Table 2. *Amount of material on the filters*

Time (hours)	Amount of material (mg)
0	<0.1
0	<0.1
0	<0.1
0.5	<0.1
0.5	<0.1
0.5	<0.1
1	<0.1
1	<0.1
1	<0.1
12	<0.1
12	<0.1
12	<0.1
24	<0.1
24	<0.1
24	<0.1
48	<0.1
48	<0.1
48	<0.1

Table 3. *Number of different sized particles per ml of solution*

	Number of particles /ml of solution			
Time (hours)	**>2 µm**	**> 5 µm**	**> 10 µm**	**> 25 µm**
0	0	0	0	0
0	0	0	0	0
0	0	0	0	0
0.5	0	0	0	0
0.5	0	0	0	0
0.5	0	0	0	0
1	0	0	0	0
1	0	0	0	0
1	0	0	0	0
12	0	0	0	0
12	0	0	0	0
12	0	0	0	0
24	0	0	0	0
24	0	0	0	0
24	0	0	0	0
48	0	0	0	0
48	0	0	0	0
48	0	0	0	0

Table 4. *Number of > 25 µm and > 10 µm sized particles per ml of solution compared to criteria's in USP <788> PARTICULATE MATTER IN INJECTIONS*

	Number of particles /ml of solution				
		USP <788> criteria*		USP <788> criteria*	Pass/Fail
Time (hours)	> 10 µm	> 10 µm	> 25 µm	> 25 µm	
0	0	≤25	0	≤3	**Pass**
0	0	≤25	0	≤3	**Pass**
0	0	≤25	0	≤3	**Pass**
0.5	0	≤25	0	≤3	**Pass**
0.5	0	≤25	0	≤3	**Pass**
0.5	0	≤25	0	≤3	**Pass**
1	0	≤25	0	≤3	**Pass**
1	0	≤25	0	≤3	**Pass**
1	0	≤25	0	≤3	**Pass**
12	0	≤25	0	≤3	**Pass**
12	0	≤25	0	≤3	**Pass**
12	0	≤25	0	≤3	**Pass**
24	0	≤25	0	≤3	**Pass**
24	0	≤25	0	≤3	**Pass**
24	0	≤25	0	≤3	**Pass**
48	0	≤25	0	≤3	**Pass**
48	0	≤25	0	≤3	**Pass**
48	0	≤25	0	≤3	**Pass**

* The criteria's used are according to USP <788> Test 1.A, "The preparation complies with the test if the average number of particles present in the units tested does not exceed 25 per ml equal or greater than 10 µm and does not exceed 3 per ml equal to or greater than 25 µm.

Conclusion

Zero (0) ≥ 25 µm particles/ml were measured, from the equipment and under the circumstances described above, at all selected time intervals.

Zero (0) ≥ 10 µm particles/ml were measured, from the equipment and under the circumstances described above, at all selected time intervals.

Compared with the criteria's set in USP <788> Test 1.A: All samples taken during the testing passed the criteria's set for number of ≥ 10 µm and ≥ 25 µm particles .

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