

PARTICULATE CONTAMINATION IN PARENTERAL SOLUTIONS

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The need to control particulate contamination in injection solutions has been recognised for many years. The particles found in solutions may be viable or non-viable. It is with this latter group that this study is concerned. Garvin and Gunner (1963) showed that it could not be assumed that terminally filtered and sterilized solutions were particle free. They also reported the presence of a wide range of different types of contaminating materials which prompt a correspondingly wide range of pharmacological responses, mostly undesirable. In recognition of this problem the Australian NBSL set a standard requiring there to be not more than 250 particles greater than 3.5 μm and that the mean plus twice the standard deviation should not exceed 500 particles to be present in each millilitre. Similar standards quickly followed in both the B.P. and U.S.P. The present standard requires not more than 1000 particles greater than 2 μm and 100 greater than 5 μm . The actual determination can be carried out by numerous methods which will give significantly different answers. The majority of the work has been carried out by Versey and Kendall (1966) and Groves and his co-workers (1964, 1969, 1971, 1977).

In this study we have re-examined a suggestion by Groves and Wana (1977) that a contamination index would represent a more suitable standard than actual numbers of particles.

Table 1 Number of particles in a solution determined by various methods

Method	Sample volume (ml)	Mean Number of Particles Greater than Size						Groves/Wana Index*	Stand. Devn.	No. Replicates
		1.4	2	5	10	20	50			
Royco 366	50	-	1215	299	80	25	2	0.149	0.009	8
H.L.A.C.	20	-	620	102	30	7	-	0.141	0.0128	10
Coulter ZB	5	592	45	4	1	-	-	0.130	0.0144	10

Groves/Wana Index (*calculated from particles per ml) where $M = \text{slope} (\log N \text{ vs } \log \text{ size})$ and $N_{1.0}$ = number of particles $> 1.0 \mu\text{m}$

$$C = \frac{\log N_{1.0} - \log 63.244}{(M)}$$

This value should not exceed 0.78 to meet B.P. specification.

It is our view that in order to accommodate a wide range of instrumental techniques for determination of particulate contamination the official standards would be more satisfactorily expressed by the use of a contamination index rather than by actual numbers of particles.

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