Regulatory Basis:
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

General Discussion

(The information from this guidance can be used by GMP sites to establish their statistical rationale for the use of this sampling plan.)

The practice of using the √N+1 as a rule for sample size is common in the pharmaceutical industry. Saranadasa noted that its use in acceptance sampling is suspect. These "accept on zero defective units" plans often carry higher than expected unacceptable quality levels (UQL) or Lot Tolerance Percent Defective (LTPD). One criticism of the plans is the lack of statistical justification. Is selecting √N+1units as a sample size ever appropriate? This guidance document will show that √N+1 sampling plans offer similar protection as some ANSI Z1.4 plans. In these cases the √N+1samplingplans can be used as an alternate approach with the confidence they carry similar risks to lot acceptability decisions.

The Military Standard plans (e.g., ANSI/ASQC Z-1.4, ISO 2859-1, & BS-6001-1 are all one & the same and conform to MIL-STD 105E) are widely accepted as statistically based sampling plans. This guidance document will show that √N+1 sampling plans offer similar protection as Military Standard plans with specified AQL levels between 1.0 and 1.5 (2.5 for the 16 to 25 lot size) percent for small lot sizes up to 150 units. In these cases the two sampling plan approaches can be used interchangeably with similar risks to lot acceptability decisions and outgoing quality.

Operating characteristic (OC) curves illustrate the probability of accepting a lot over varying percent defective rates (Figure 1). When evaluating sampling plans, two points on the curve are of primary interest: the defective rate when lots will be routinely passed and the defective rate when lots will be routinely failed. It is fairly common to use the 95% probability of accepting a lot as the routinely passing point and the defective rate is called the acceptable quality level or limit (AQL). Lots with a defective rate at or below the AQL would be expected to pass the sampling plan criteria 95% of the time. The 10% probability of accepting a lot is typically used as the failing point and the defective rate is commonly called the unacceptable quality level (UQL) or lot tolerance percent defective (LTPD). Lots with a defective rate at or above the UQL would be expected to pass the sampling plan criteria 10% of the time (fail 90% of the time). The

AQL and UQL of any sampling plan can be used to assess the risk in deciding whether a lot is acceptable.

Sampling plans with similar AQL and UQL levels or the entire OC curve offer similar protection against the risk of an incorrect lot acceptability decision. Figures 2-5 show the OC curves for √N+1 and the Military Standard for normal, general level-II inspection for the lot size categories

√N+1 Sampling Plans versus Military Standard for Lot Size 16 to 25 (Code C)

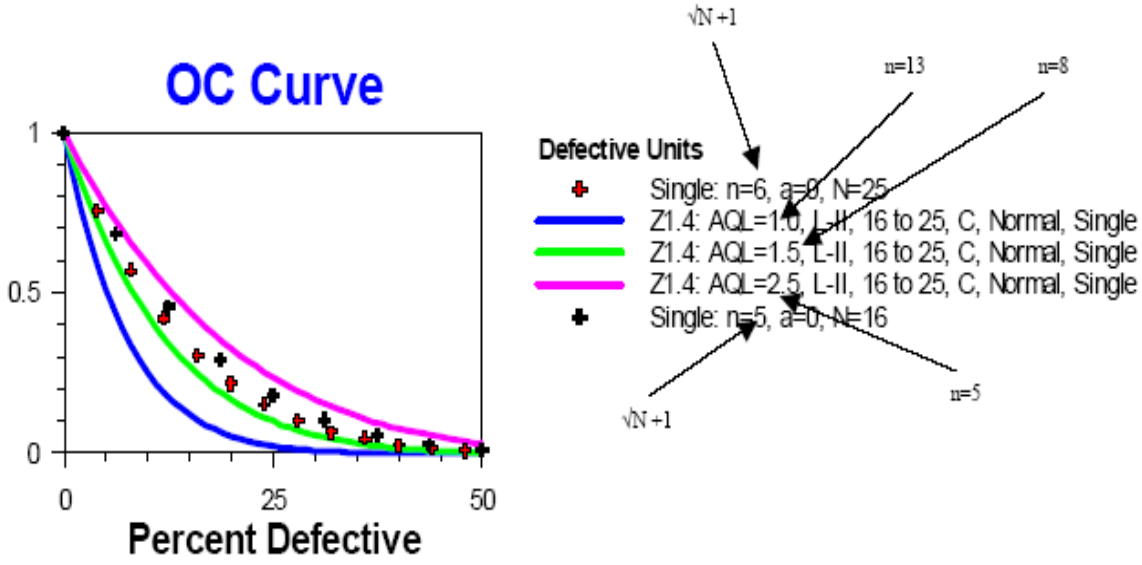

Figure 2

How similar are the √N+1 plans and the Military Standard? For the most part the √N+1 curves are bracketed by Military Standard plans with AQL levels between 1.0 and 1.5. The exception is shown above for the 16 to 25 lot size where the AQL of 2.5 must be used to bracket the √N+1 plans.

√N+1 Sampling Plans versus Military Standard for Lot Size 91 to 150 (Code F)

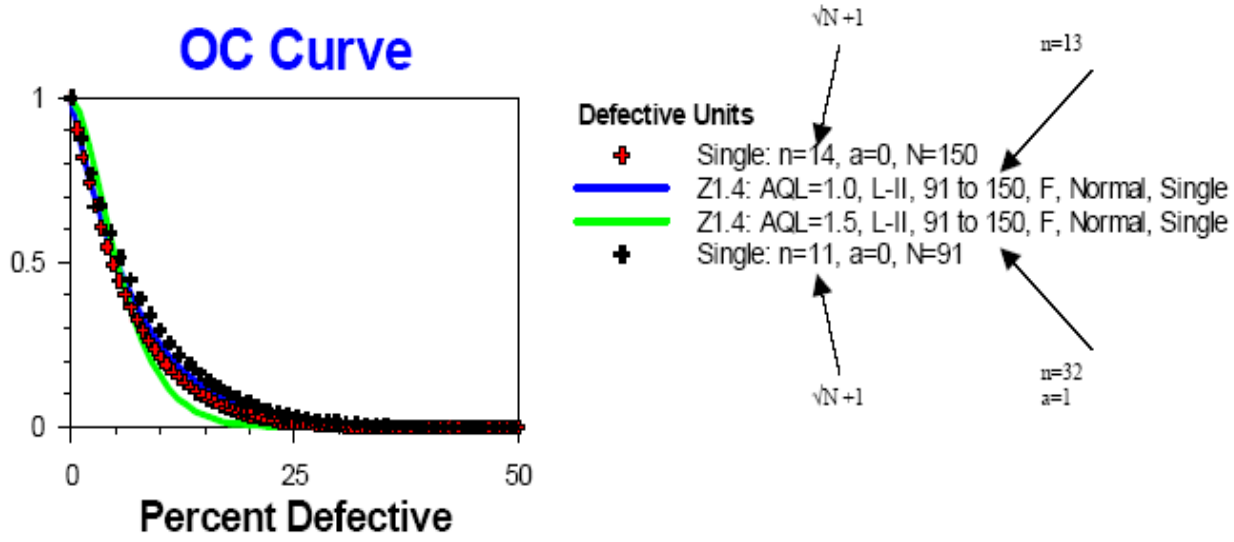

Figure 5

In the next higher lot size category the curves almost lie on top of each other; once again illustrating the similarity of the MIL-STD and √N+1 plans when the AQL is chosen between 1.0 and 1.5. Note the AQL=1.5 plan allows 1 defective unit to be found in 32 samples and still pass the lot. All other plans here and in the lower lot sizes are accept on zero defects in the sample plans.

Plan Summaries

Table 2				Table 3			
Sampling Plans	AQL	LTPD	AOQL	Sampling Plans	AQL	LTPD	AOQL
√N+1 plan: Single: n=14, a=0, **N=150**	0.36	14.67	2.54	√N+1 plan: Single: n=11, a=0, **N=90**	0.45	18.89	3.23
Z1.4: **AQL=1.0**, L-II, **91 to 150**, F, Normal, Single, n=13, a=0	0.39	16.23	2.73	Z1.4: **AQL=1.0**, L-II, **51 to 90**, E, Normal, Single, n=13, a=0	0.39	16.23	2.73
Z1.4: **AQL=1.5**, L-II, **91 to 150**, F, Normal, Single, n=32, a=1	1.12	11.62	2.60	Z1.4: **AQL=1.5**, L-II, **51 to 90**, E, Normal, Single, n=8, a=0	0.64	25.01	4.33
√N+1 plan: Single: n=11, a=0, **N=91**	0.45	18.68	3.23	√N+1 plan: Single: n=9, a=0, **N=51**	0.56	21.57	3.78

Table 4				Table 5			
Sampling Plans	AQL	LTPD	AOQL	Sampling Plans	AQL	LTPD	AOQL
√N+1 plan: Single: n=9, a=0, **N=50**	0.56	22.00	3.81	√N+1 plan: Single: n=6, a=0, **N=25**	0.83	32.00	5.90
Z1.4: **AQL=1.0**, L-II, **26 to 50**, D, Normal, Single, n=13, a=0	0.39	16.23	2.73	Z1.4: **AQL=1.0**, L-II, **16 to 25**, C, Normal, Single, n=13, a=0	0.39	16.23	2.73
Z1.4: **AQL=1.5**, L-II, **26 to 50**, D, Normal, Single, n=8, a=0	0.64	25.01	4.33	Z1.4: **AQL=1.5**, L-II, **16 to 25**, C, Normal, Single, n=8, a=0	0.64	25.01	4.33
√N+1 plan: Single: n=7, a=0, **N=26**	0.71	26.92	4.49	Z1.4: **AQL=2.5**, L-II, **16 to 25**, C, Normal, Single, n=5, a=0	1.02	36.90	6.70
				√N+1 plan: Single: n=5, a=0, **N=16**	1.00	37.50	7.16

