THE STUDY OF THE PERFORMANCE OF MICROSPACER USING THE CASCADE IMPACTOR

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Objective

Determine the comparative deposition of albuterol in an Anderson Mk 1 cascade impactor using a 'standard' metered dose inhaler (MDI) with and without connection to a prototype 'microspacer'.

Methods

The Anderson Mk I cascade impactor was employed to 'simulate' the lung. A plastic throat was employed to simulate the oro-pharyngeal region of the respiratory system and was connected to the top of a cascade impactor (**figures 1 & 2**). The microspacer was connected to a Proventil MDI and after priming was attached to the plastic throat as shown in figures 1 and 2. The MDI was actuated 5 times (≈450μg) in the horizontal position while the cascade impactor was running (28.3Liters/min ambient air). Each stage of the impactor was then cleaned with a microwipe containing 100 μl of 0.1M NaOH which was then placed in glass vials and diluted to 5ml with further 0.1M NaOH. The plastic throat and microspacer were also washed out thoroughly with 10 and 20ml of NaOH respectively. Samples were then analyzed directly in 1cm pathlength quartz cuvettes using a Gilford "Response" UV/visible spectrophotometer at a wavelength of 243nm at a temperature of 25^{0}C. The frequency distribution, mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD), assuming a log-normal distribution of particulate matter, were obtained from the data. The protocol was repeated without the presence of the microspacer.

Results

The basic comparative data is summarized in table 1. A wavelength scan of the albuterol is shown in figure 3 indicating that a useful peak for analysis exists at 243nm. The mass frequency

distributions of the particles deposited in the cascade impactor, in the presence and absence of the microspacer, are shown in figures 4 and 5. The MMAD and GSD results are given in table 2 and indicate that there is little difference in the mean diameters of the particles which reach the impactor. The deposited particles in the presence and absence of the microspacer are highly polydisperse (GSD>2.5) but log-probability data of size vs cumulative % undersize as shown in figures 6 through 15 and show that the deposited particles tend to follow a log normal distribution. The presence of the microspacer resulted in a 3.3x reduction of the actuated dose reaching the plastic 'artificial' throat due to retention of albuterol on the screen and tubing of the spacer. The quantity of albuterol depositing in the impactor was not significantly different when the spacer was used (table 1).

Discussion and conclusions

Visual observation of an acuated MDI with and without the microspacer indicated that differences in the nature of the aerosolized dose existed. The use of the cascade impactor and artificial throat imply that the spacer acts to prevent a portion of the actuated dose from reaching the plastic throat while allowing the smaller end of the droplet/particle distribution to leave MDI and presumably reach the lung. The screen itself may also act as an impaction surface for droplets which are not completely evaporated and therefore may also contribute to the resulting particle size distribution as it passes across the screen. The MDI alone caused a large portion of the albuterol to deposit in the plastic throat. The results are similar to those which would be expected when other spacers such as the aerochamber and inspirease are employed, although the mechanisms of retention are somewhat different (sedimentation and impaction vs impaction). Since it appears that the screen functions primarily by blocking a portion of the actuated dose good quality control should be built into the device as variations in screen size are likely to markedly affect the amount of an actuated dose which can be expelled from the screen. It is worth further study to estimate what screen sizes

would be optimal. In conclusion, from the results with the impactor, it can be implied that in human use the Microspacer may reduce the quantity of actuated dose which will impact in the extrathoracic regions of the respiratory tract relative to using an MDI alone. For the vast majority of asthmatics who lead relatively normal lives the microspacer may prove to be a socially convenient and therapeutically useful device.

Table 1. Comparative data for the performance of the Microspacer

MEASURED PARAMETER	WITH SPACER	WITHOUT SPACER	SIGNIFICANCE[a]
Mean total of albuterol in impactor[b]	12.45 (2.78)	13.75 (2.43)	NS
Mean total of albuterol in throat	3.15 (1.14)	10.38 (1.88)	$p<0.0001$
MMAD (GSD)[c]	2.33 (3.19)	1.98 (2.62)	NS

a Significance based upon 5% significance level ($\alpha=0.05$)

b Mean totals are based upon unitless values. Values are the mean ± standard deviation in parenthesis. N=5

c Results are the mass median aerodynamic diameter (MMAD) ± the geometric standard deviation (GSD) in parenthesis. The use of GSD assumes that the particles follow a log normal distribution

Table 2. MMAD and (GSD) data for the particles deposited in the cascade impactor

Expt #	WITH SPACER	WITHOUT SPACER
1	2.6 (2.6)	2.1 (2.0)
2	2.5 (3.6)	1.9 (3.3)
3	2.2 (4.0)	1.5 (3.3)
4	2.1 (3.2)	2.2 (2.2)
5	2.3 (2.6)	2.4 (2.3)
MEAN	2.3 (3.2)	2.0 (2.6)

Table 3. Microspacer vs Azmacort

MEASURED PARAMETER	MICROSPACER	AZMACORT	SIGNIFICANCE[a]
Mean total of albuterol in impactor[b]	12.45 (2.78)	11.25 (3.91)	NS
Mean total of albuterol in throat	3.15 (1.14)	3.30 (1.10)	NS
MMAD (GSD)[c]	2.33 (3.19)	2.09 (2.59)	$p<0.05$

a Significance based upon 5% significance level ($\alpha=0.05$)

b Mean totals are based upon unitless values. Values are the mean ± standard deviation in parenthesis. N=5

c Results are the mass median aerodynamic diameter (MMAD) ± the geometric standard deviation (GSD) in parenthesis. The use of GSD assumes that the particles follow a log normal distribution

FIGURE 1 : DEPOSITION STUDY WITHOUT SPACER

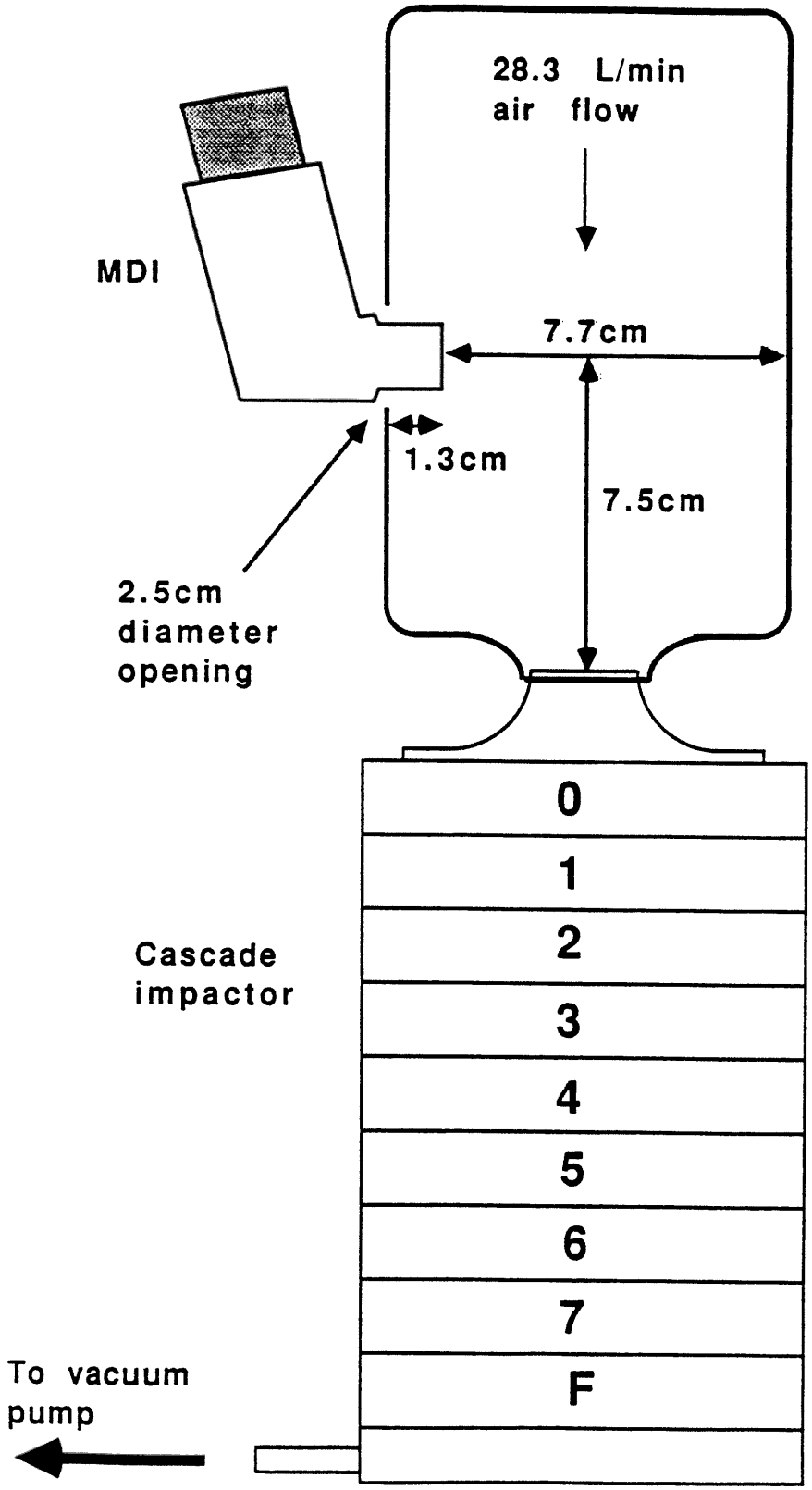
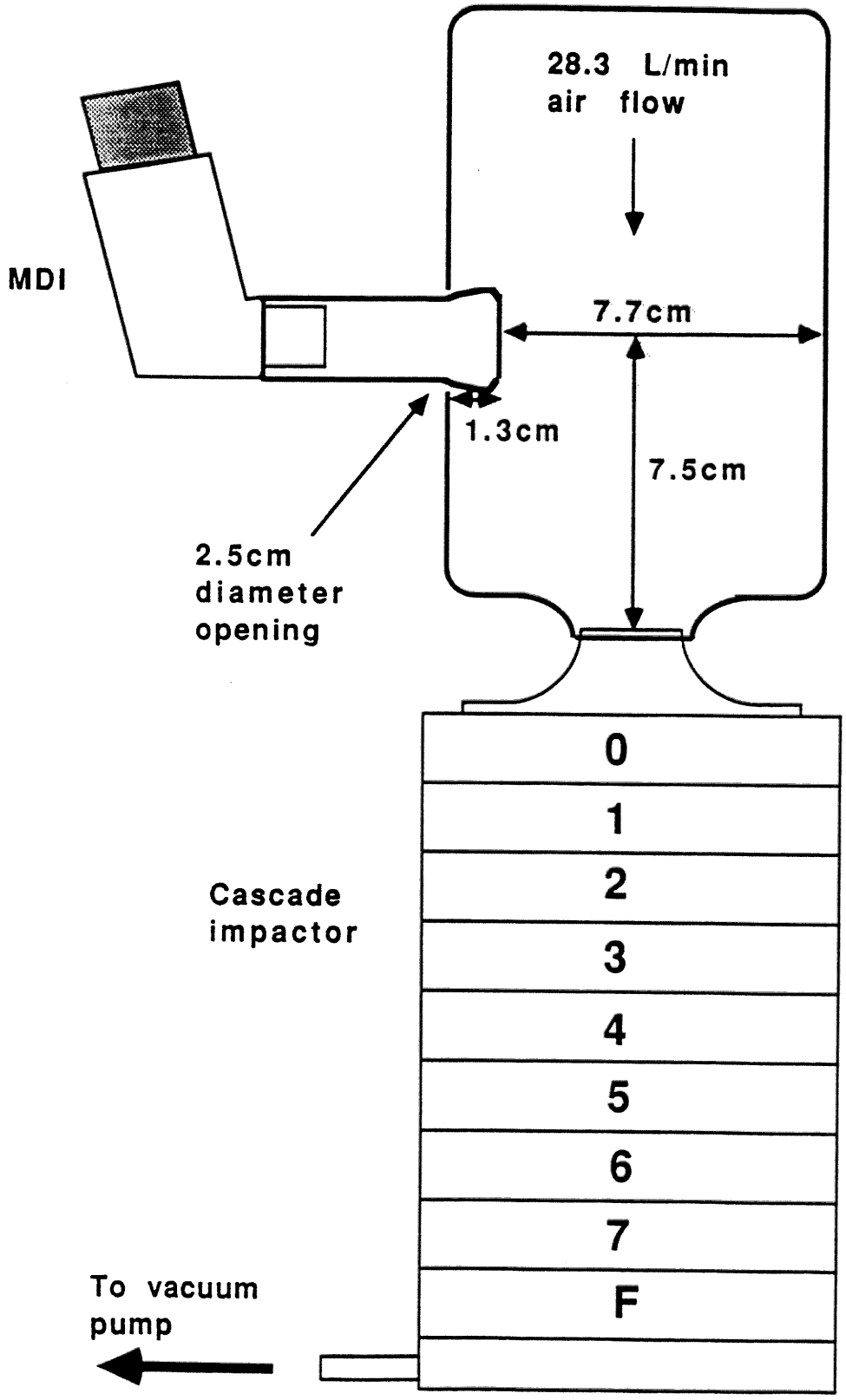


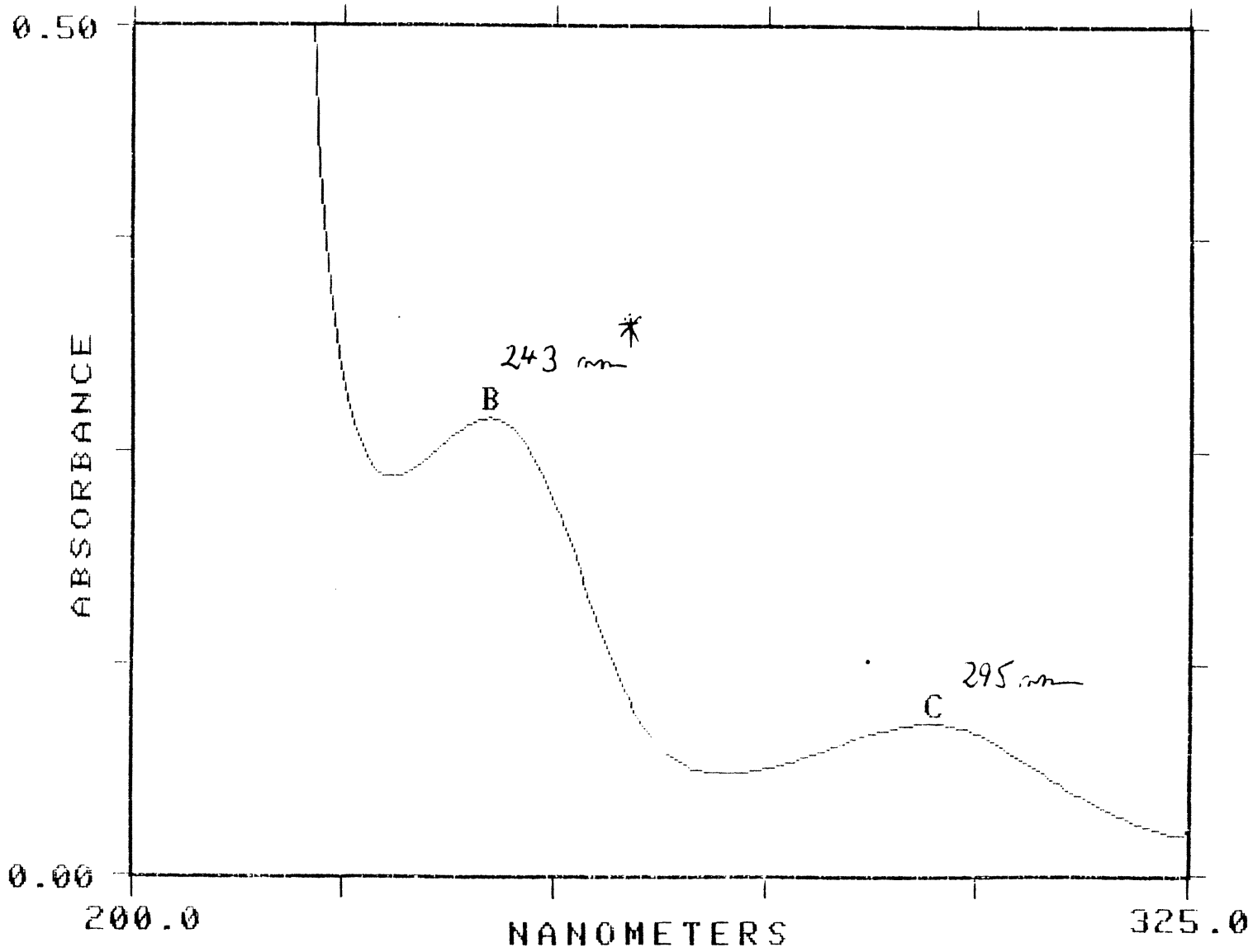
FIGURE 2 : DEPOSITION STUDY WITH SPACER



GILFORD "RESPONSE" UV SPECTROPHOTOMETER.

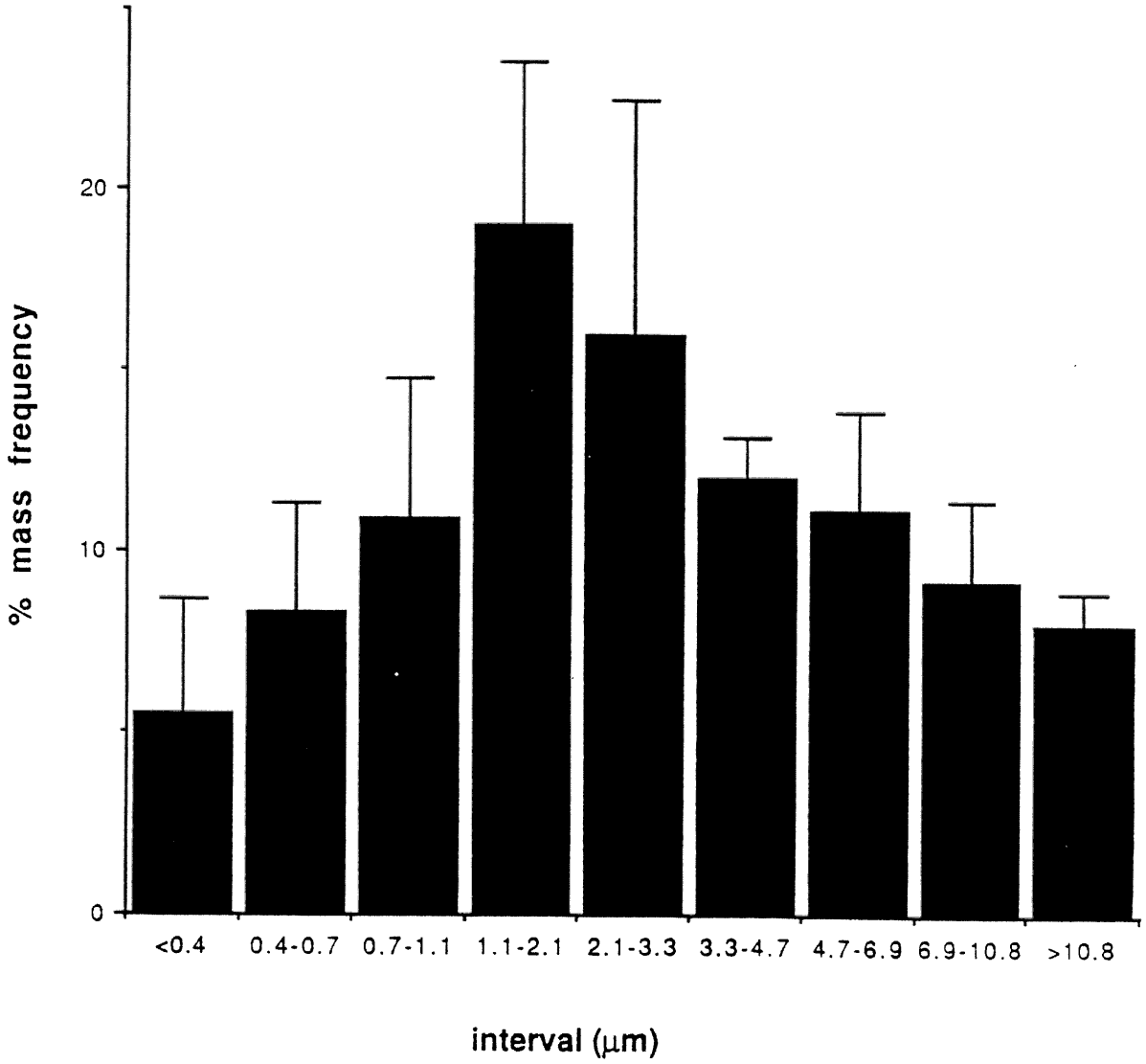
ANALYSIS = λ SCAN OF ALBUTEROL (PROVENTIL) ~ 5 μg/ml

SAMPLE = 1



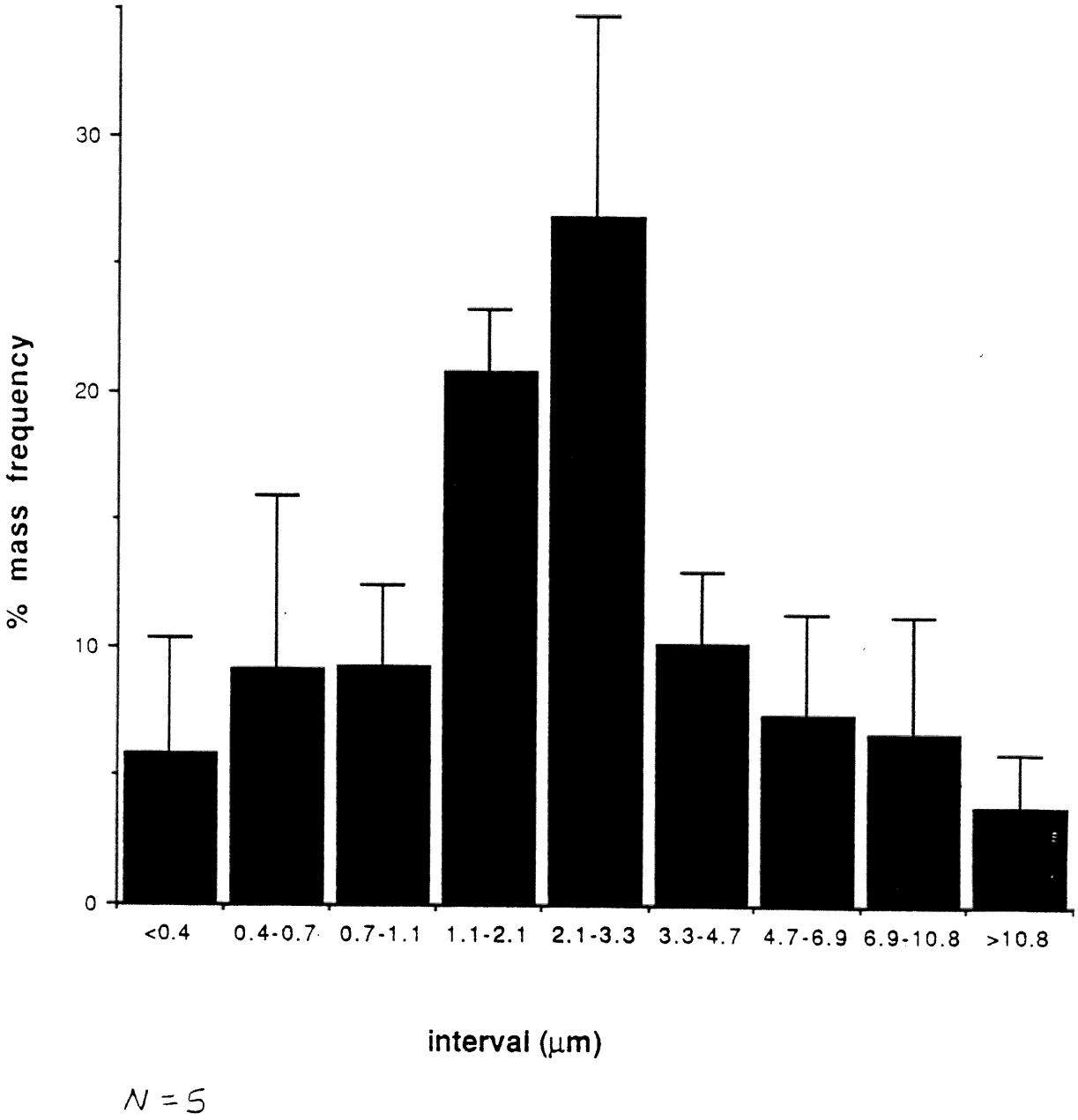
* λ USED FOR SAMPLE ANALYSIS

Mean frequency distribution (with spacer)



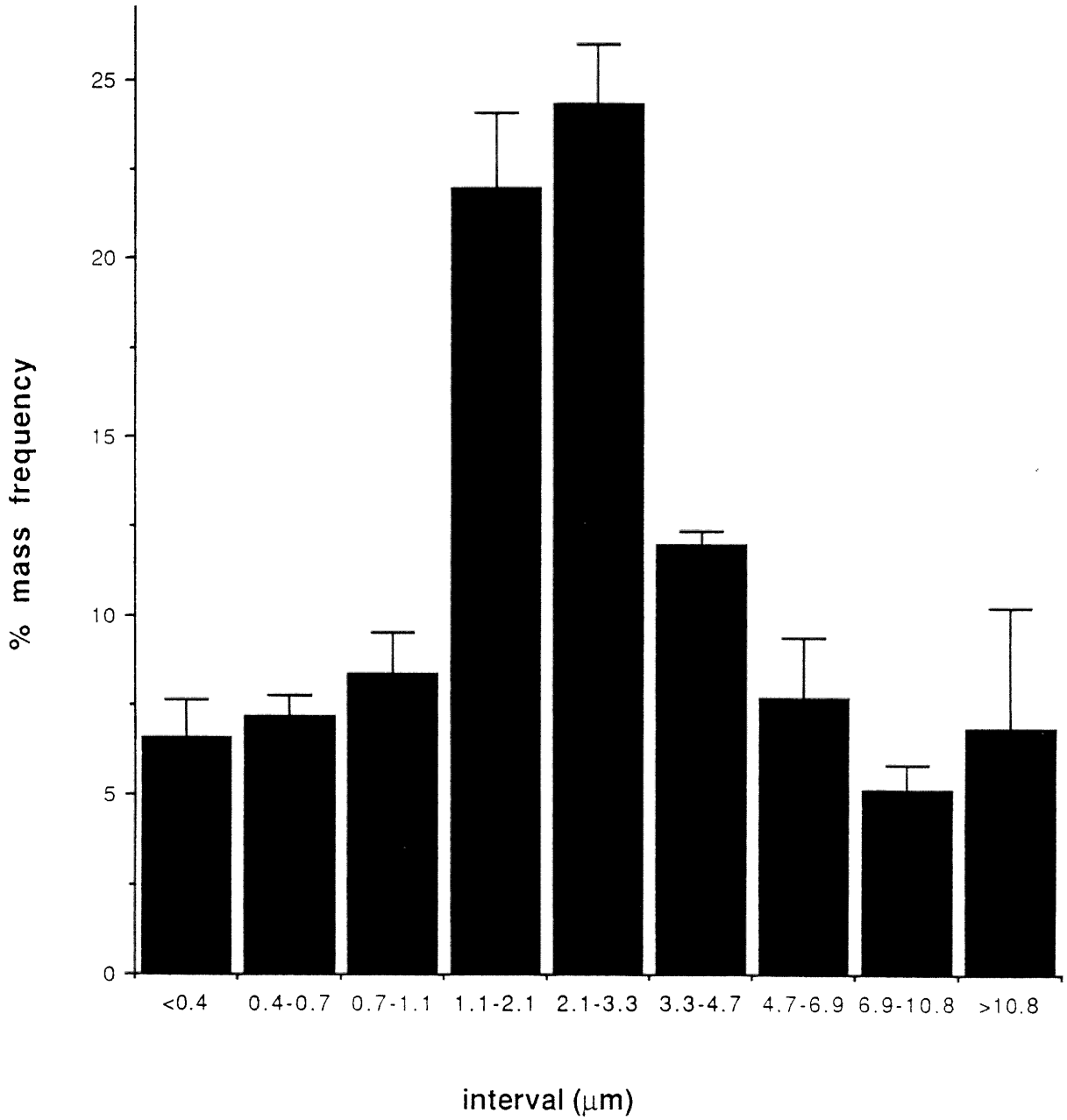
N = 5

Mean frequency distribution (without spacer)



N = 5

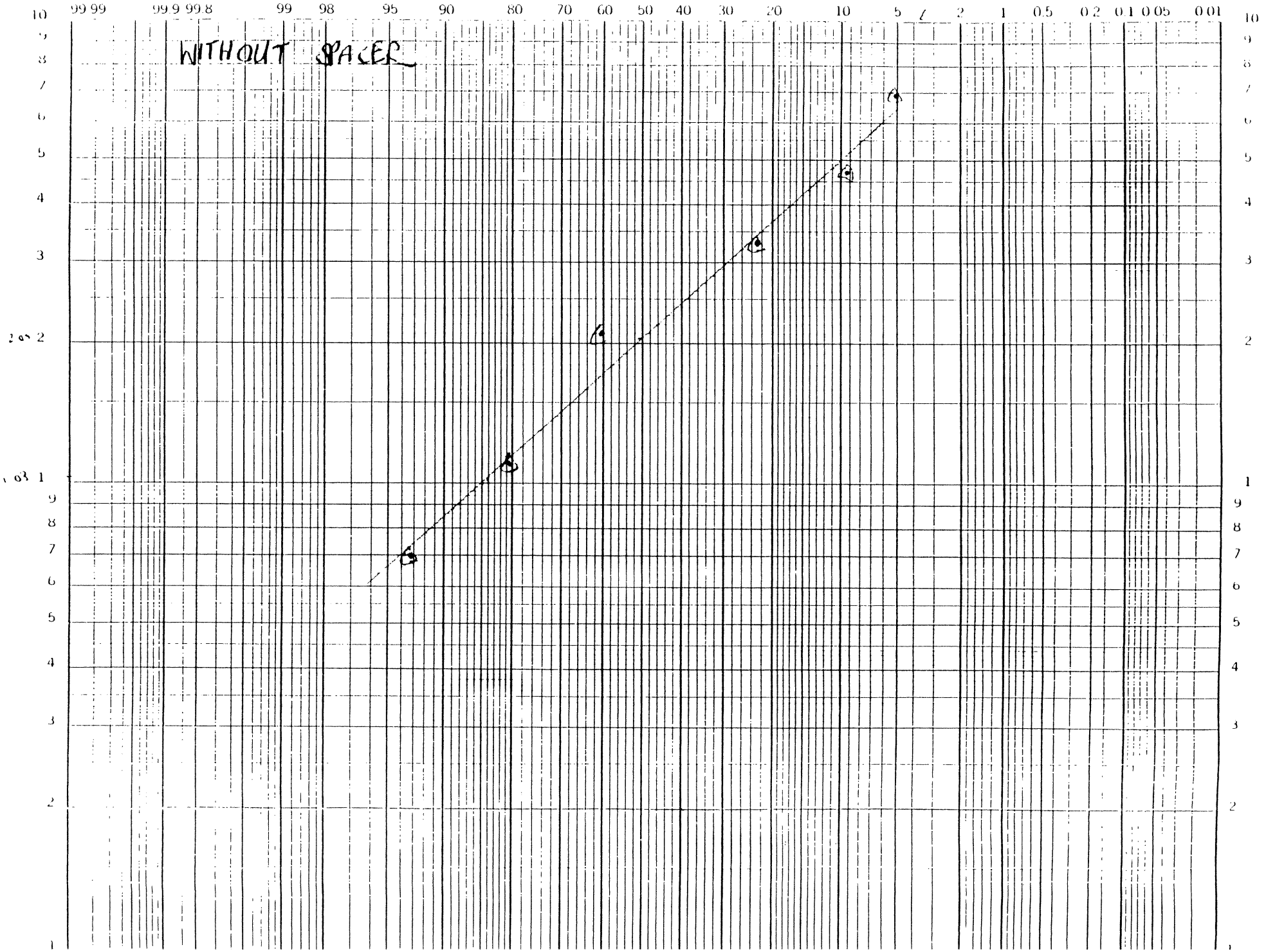
Mean frequency distribution (Azmacort)



(1)

PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO.

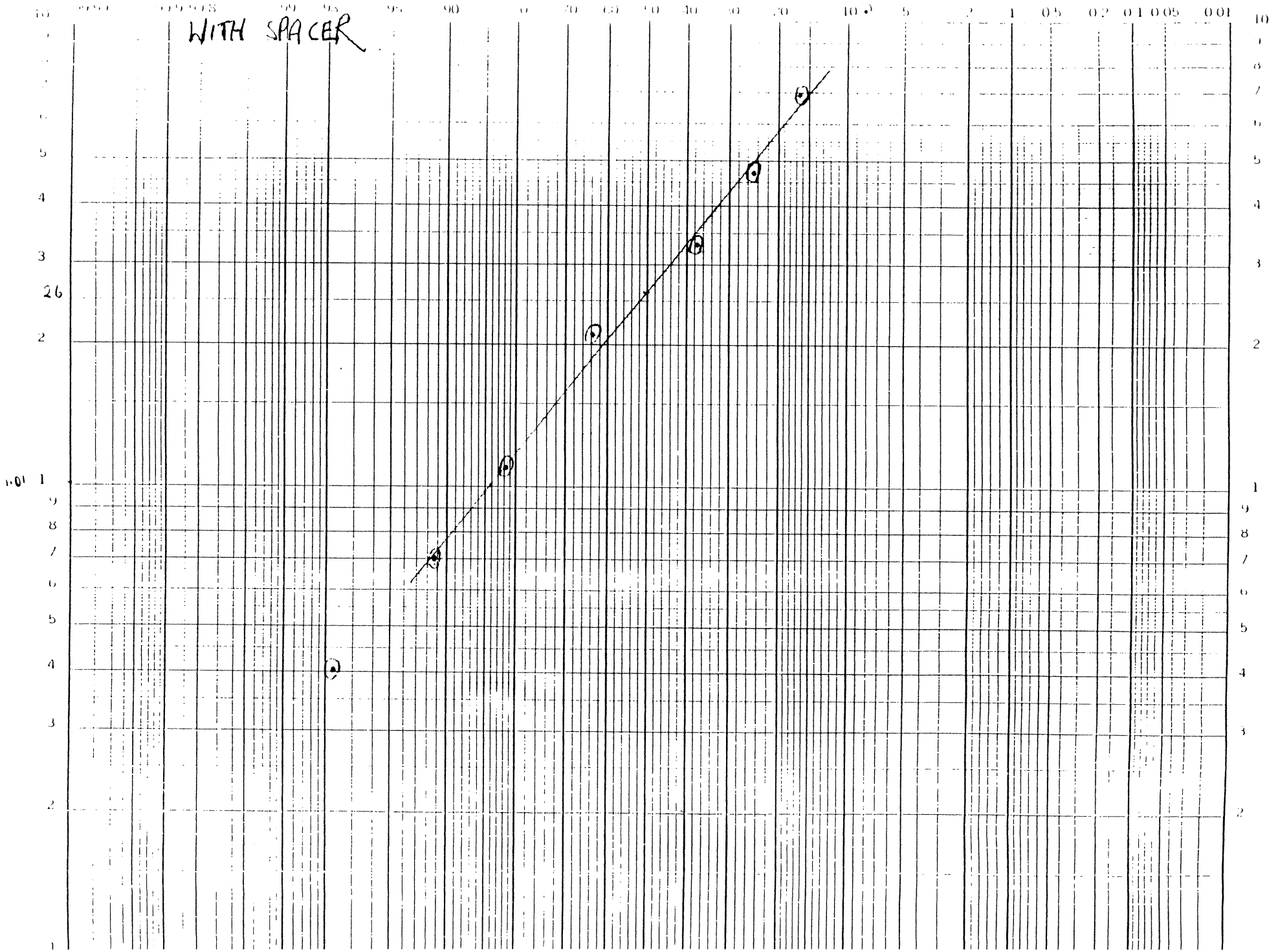
46 8040



(1)

PROBABILITY × 2 CYCLE CHARTS
KEUFFEL & ESSER CO.

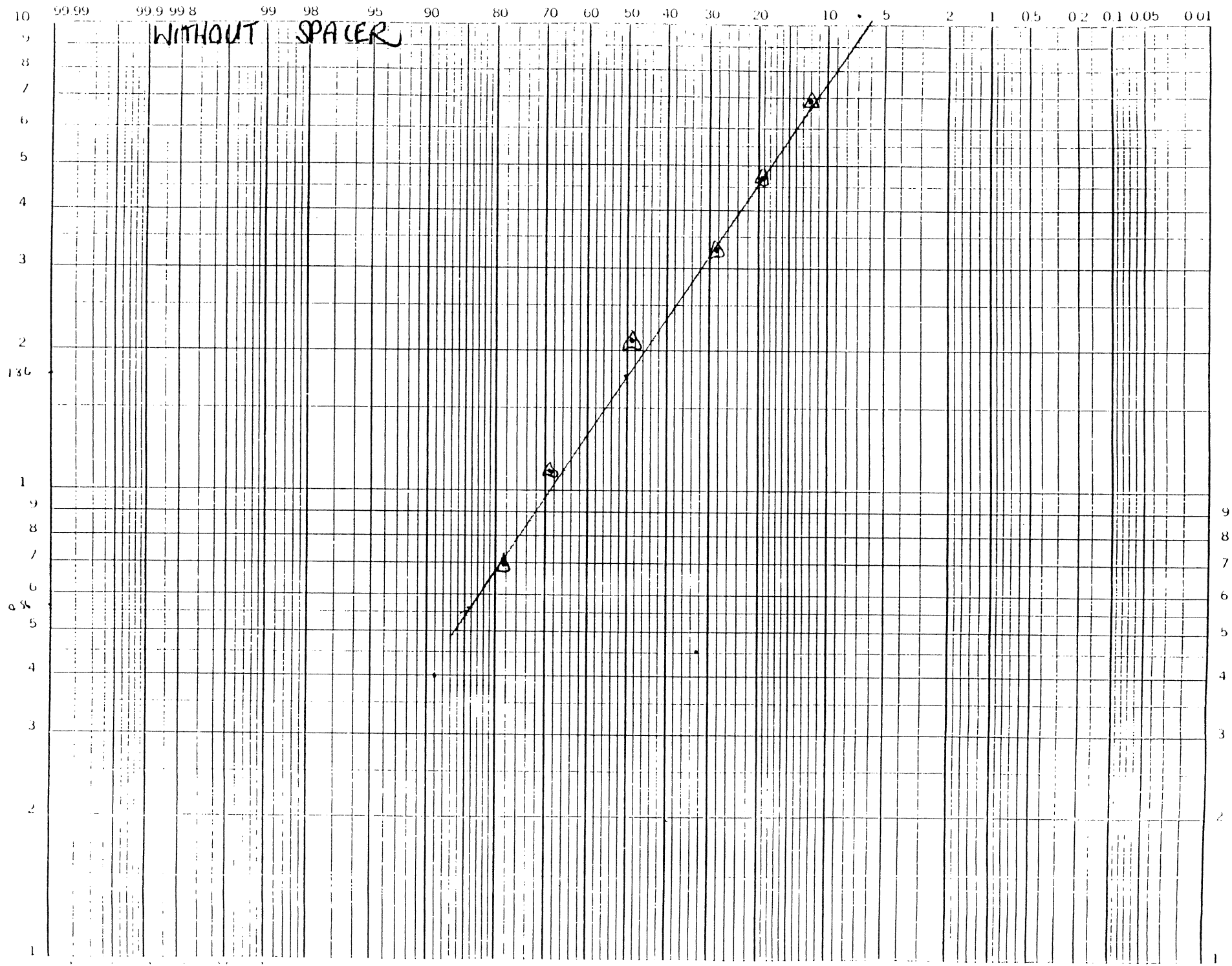
46 8040



(2)

K&E PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO

46 8040



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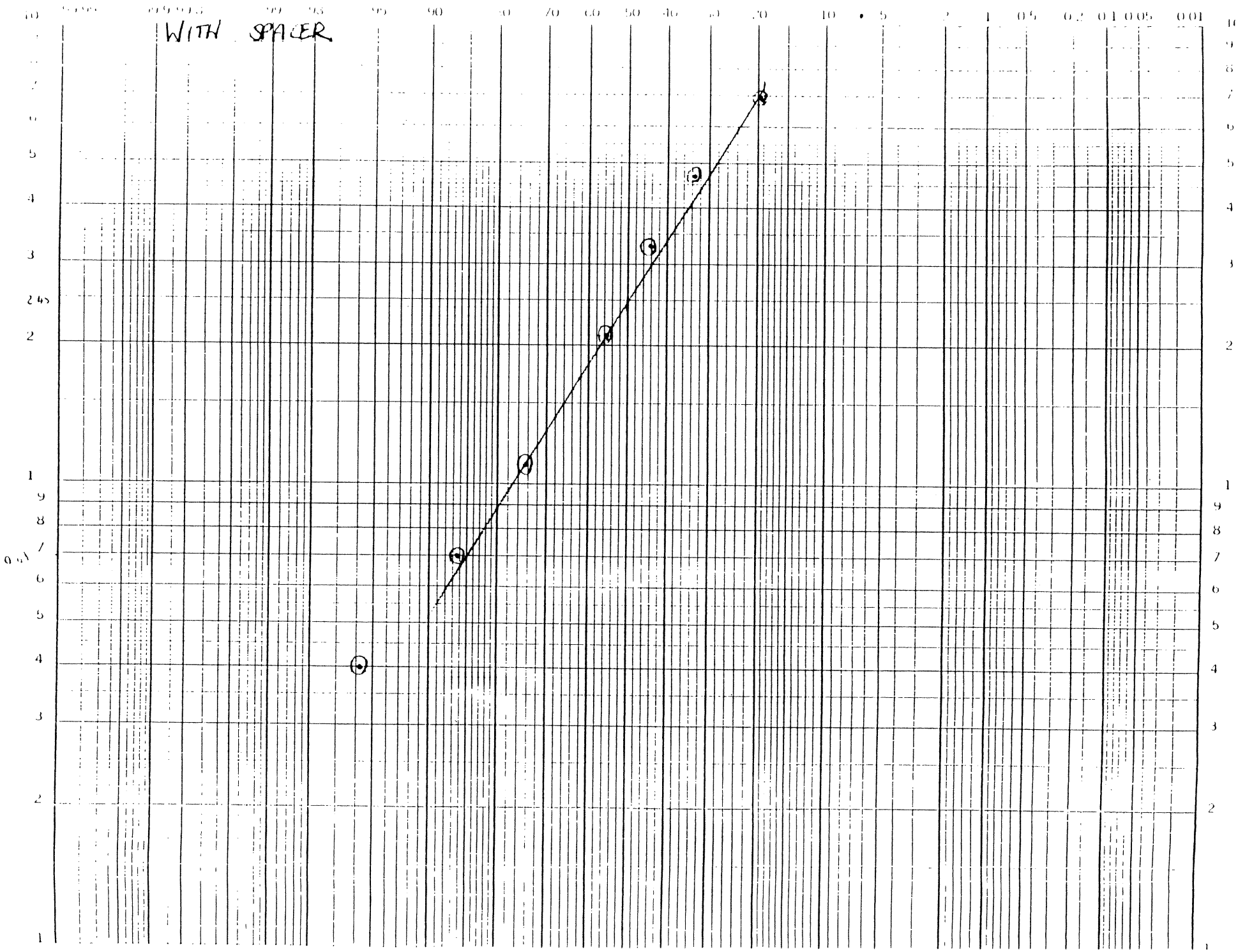
PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO.

46 8040



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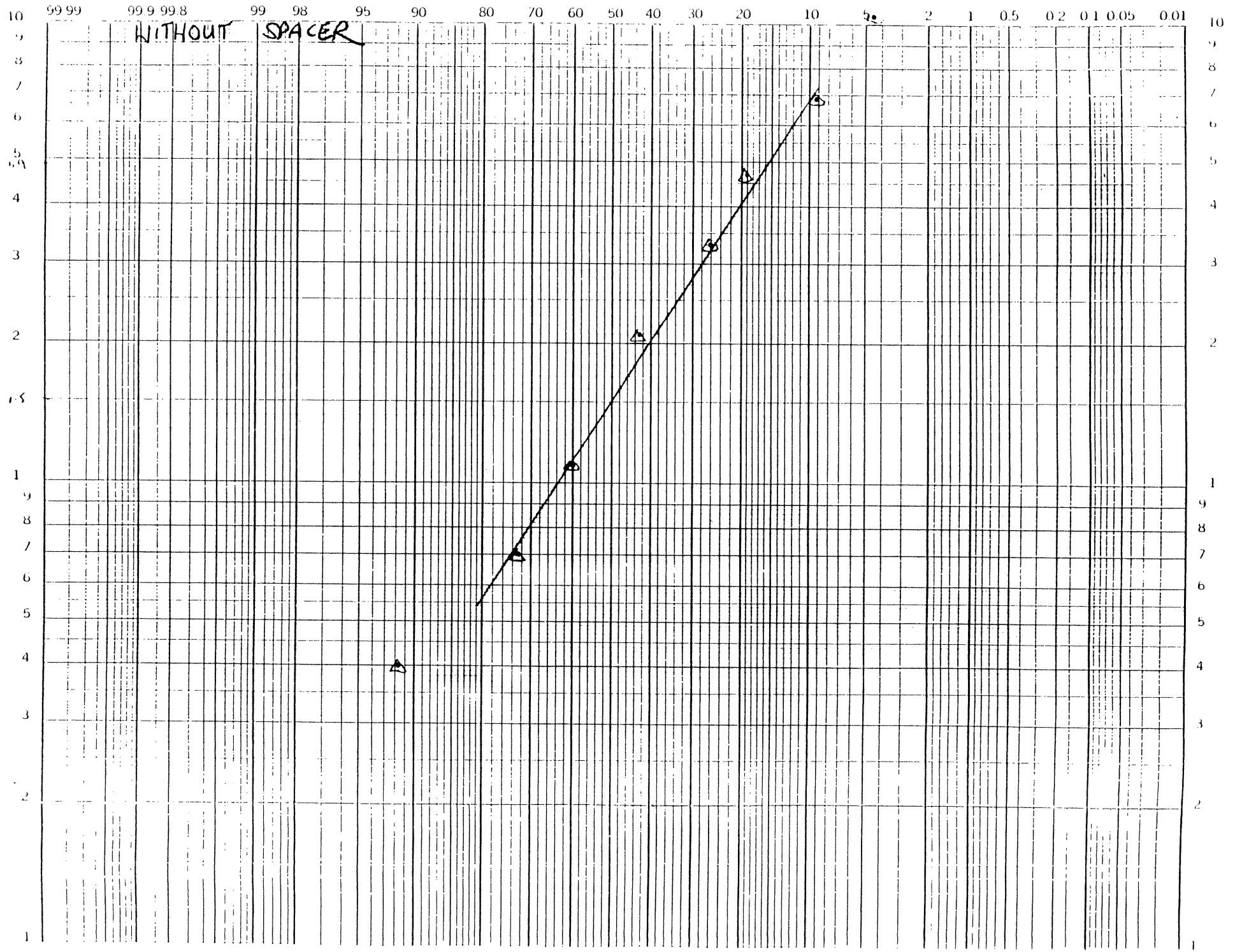
K&E PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO

46 8040



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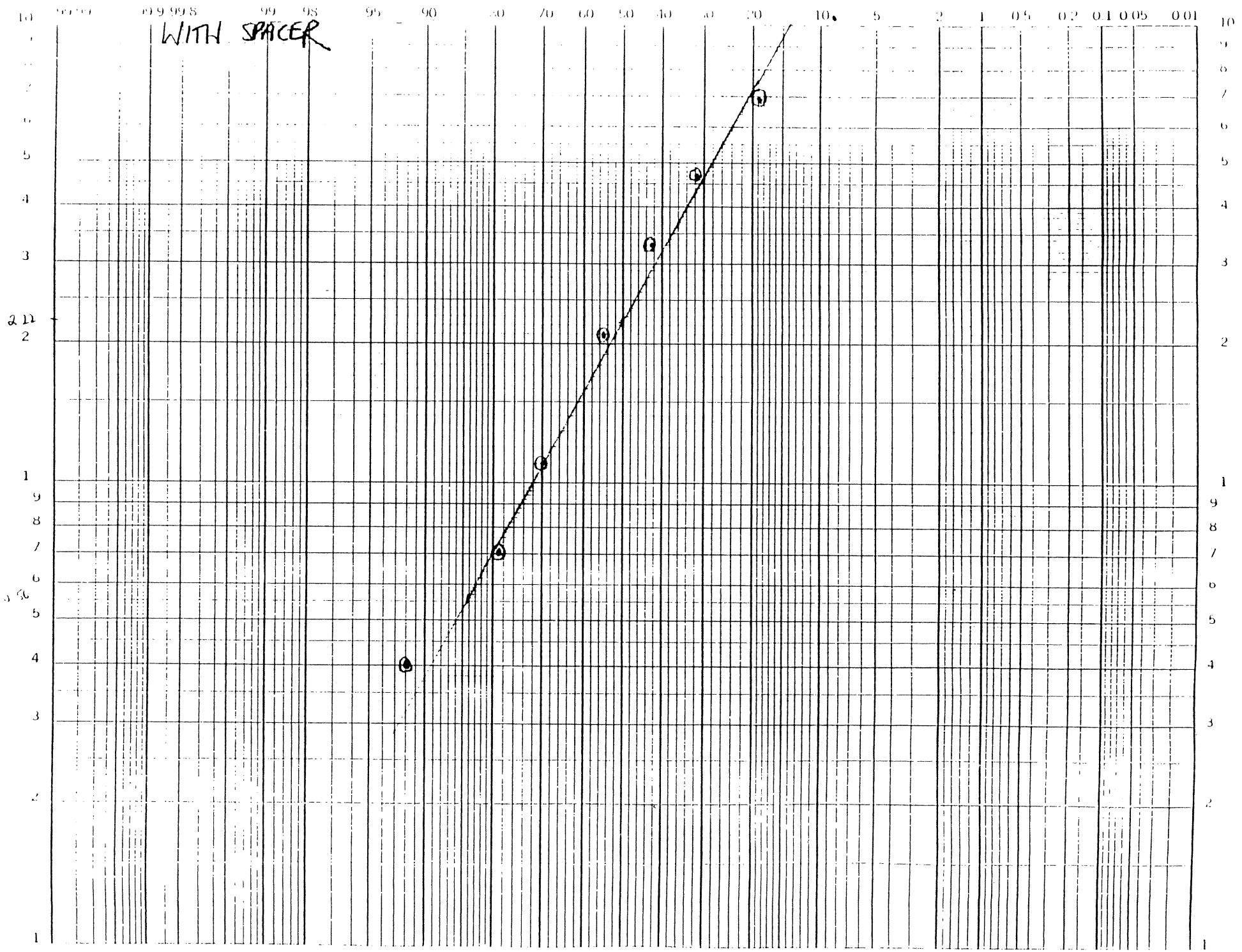
PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO.

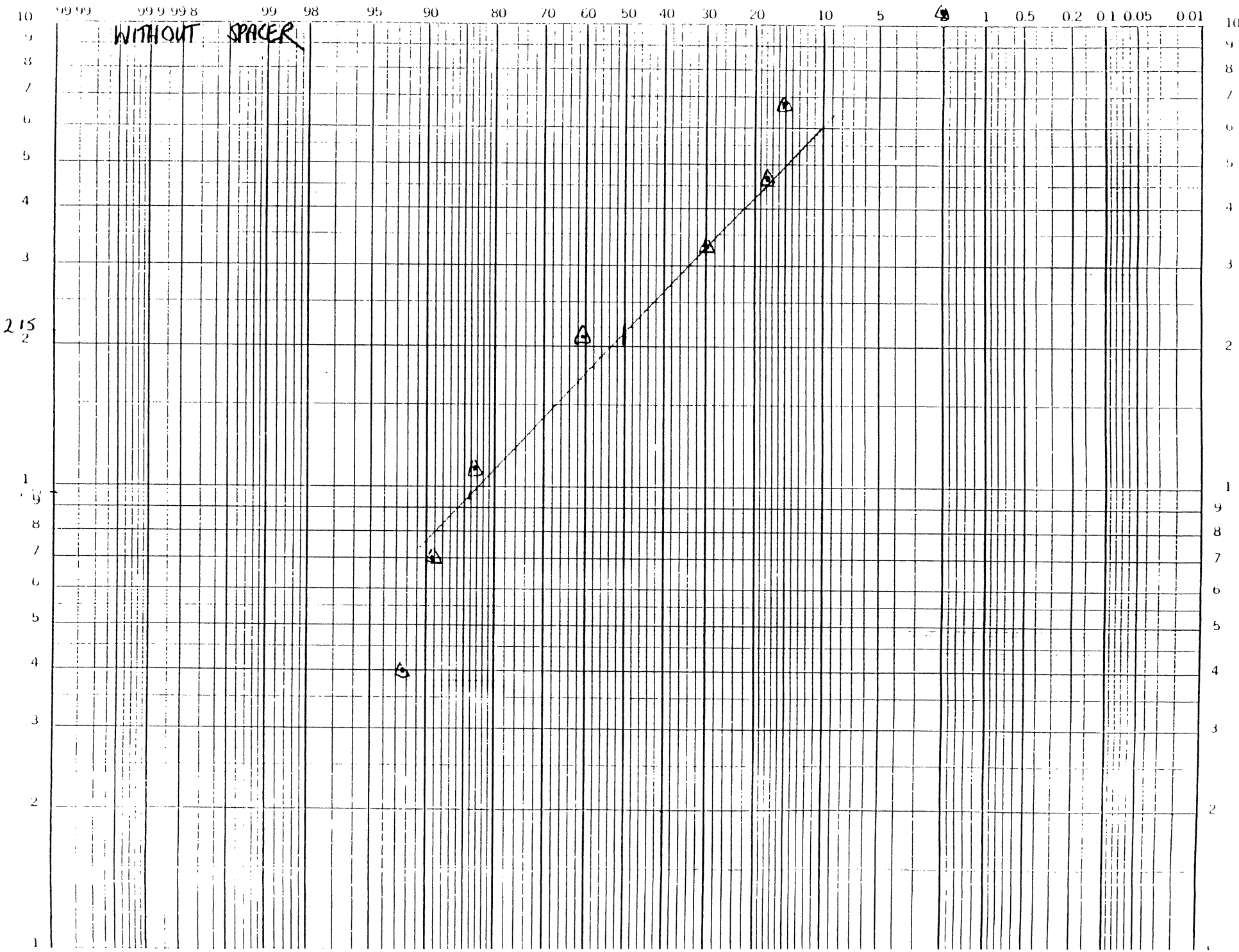
46 8040



(4)

PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO.

46 8040



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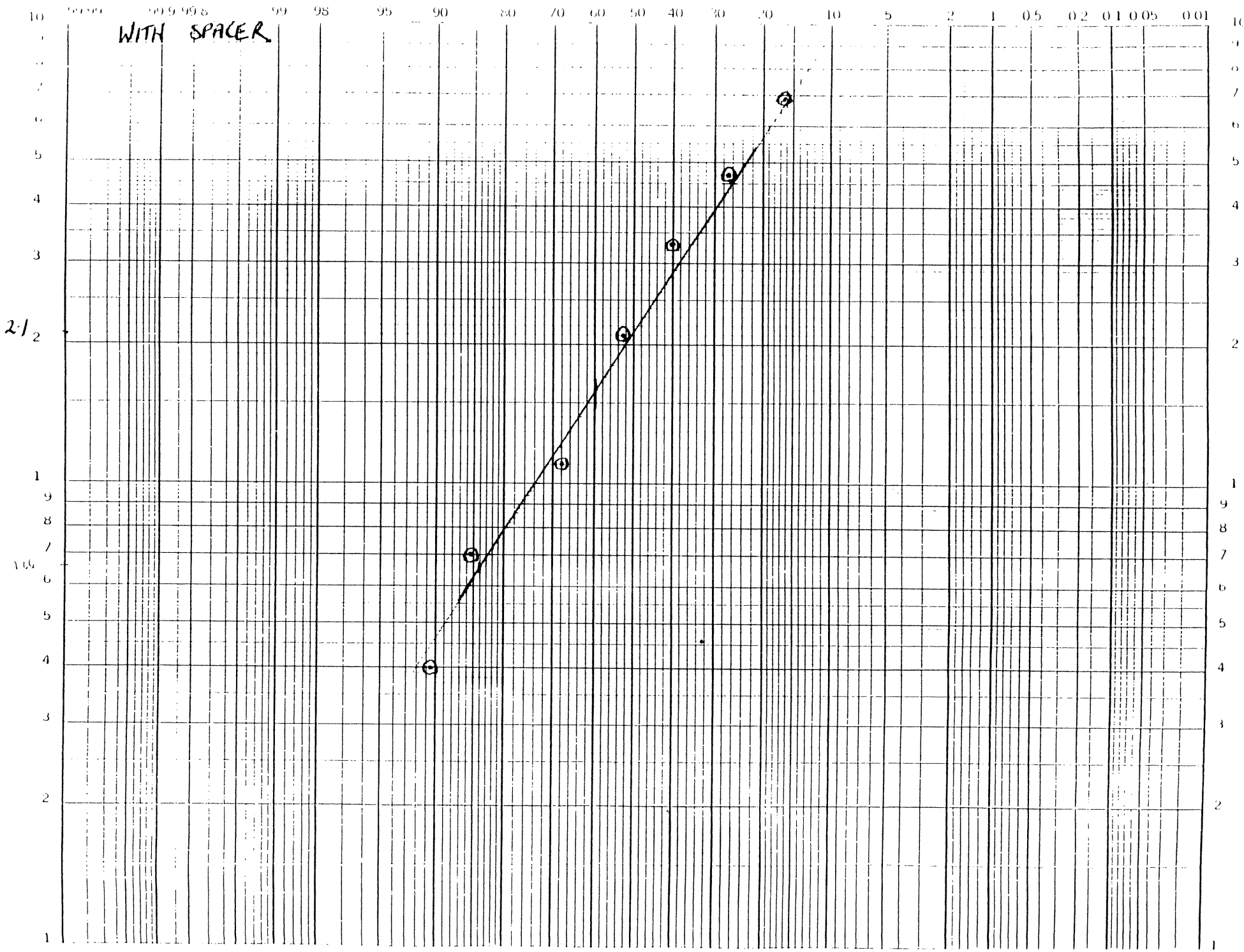
PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO.

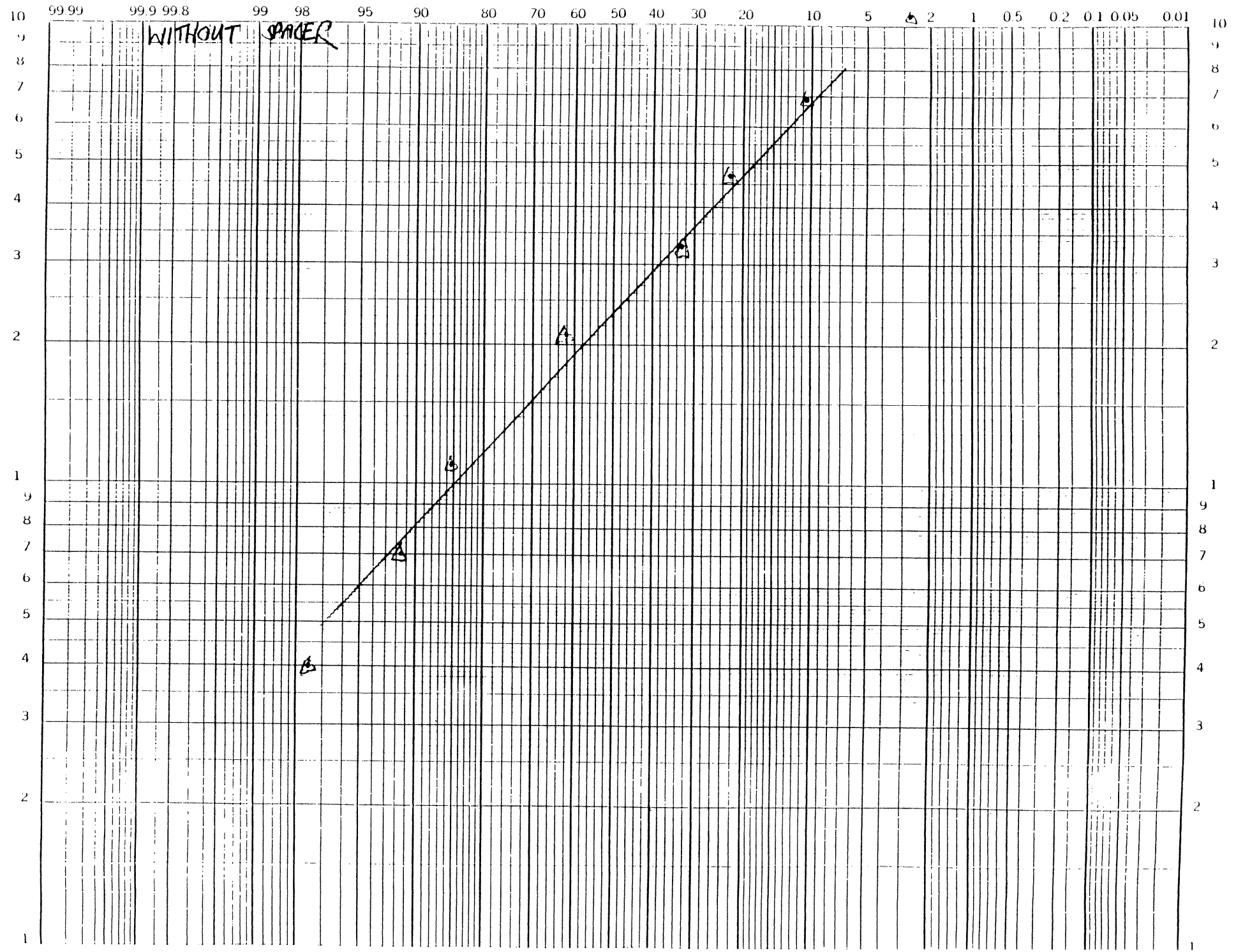
46 8040



(5)

K+E PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO MADE IN U.S.A.

46 8040



(5)

K+E PROBABILITY X 2 LOG CYCLES
KEUFFEL & ESSER CO

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