Tablet Acceptance by a Double Sampling Plan

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A double sampling plan for tablet acceptance is presented and analyzed. The answers to three fundamental questions are presented: (*a*) How will the plan operate with respect to batches of tablets which vary in quality from batch to batch? (*b*) What will be the quality of tablets passed into stock by the plan? (*c*) How much inspection on the average will the plan require?

IN THE PRODUCTION of coated aspirin tablets intended to be used for sustained-release action, lot sizes of 500 tablets were produced. A double sampling plan was selected ($n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$). The authors were interested in analyzing the ability of this plan with respect to the three fundamental features listed below.

(*a*) How will the plan operate with respect to batches of tablets which vary in quality from batch to batch?

(*b*) What will be the quality of tablets passed into stock by the plan?

(*c*) How much inspection on the average will the plan require?

The first question is answered by the operating characteristic (OC) curve for the plan. The second question is answered by the average outgoing quality (AOQ) curve for the plan and the third question by the average sample number (ASN) curve and the total amount of inspection (TAI) curve for the plan.

This paper is intended to show how to construct, by approximate methods, these curves for our double sampling plan.

DISCUSSION

Because sampling is a problem involving the laws of chance, the development of good sampling acceptance schemes requires consideration of the mathematics of probability.

Three probabilities must be noted:

(*a*) The probability of the joint occurrence of two independent or dependent events is the *product* of their respective probabilities. Thus, if a coin *and* a die are tossed simultaneously, the probability of a head *and* an ace is $^1/_2 \times ^1/_6 = ^1/_{12}$.

(*b*) The probability that one or the other of a set of mutually exclusive events will occur on an occasion where any of them may occur is the *sum* of their respective probabilities. Thus, the probability of a 7 *or* an 11 at one toss of two dice is $^1/_6 + ^1/_{18} = ^2/_9$.

(*c*) The Poisson exponential will be used to approximate the more rigorously correct probabilities given by the binomial formula.

The probability (1) of finding m defects in a random sample of n pieces drawn from an infinite universe (general output of uniform product) in which the fraction defective is p, is given exactly by the $m + 1$st term of the expansion of the binomial, $[(1 - p) + p]^n$, $P_{m,n,p} = C_m^n(1 - p)^{n-m}p^m$ (Eq. 1)

When $p < 0.10$, a good approximation to Eq. 1 is given by the $m + 1$st term of the Poisson exponential distribution

$$P_{m,n,p} \approx P_{m,pn} = \frac{e^{-pn}(pn)^m}{m!}$$

The first study concerned the tablet weight (a nondestructive test) for which we constructed OC, AOQ, ASN, and TAI curves. The second study was for tablet disintegration, for which only the OC and ASN curves are used since this is a destructive test.

Operating Characteristic (OC) Curve.—(Table I, Fig. 1).—In our plan a 50-tablet sample ($n_1 = 50$) was taken. In testing for tablet weight on the 50-tablet sample, the batch was acceptable if all tablets passed the weight test ($c_1 = 0$). If all the tablets did not pass the weight test a 100-tablet sample ($n_2 = 100$) was tested, and the batch was acceptable if two tablets ($c_2 = 2$) or less did not pass the weight test in the first and second sample of 150. In the second study, on running U.S.P. XVI disintegration tests for coated tablets on a 50-tablet sample, the batch was acceptable if all tablets dissolved ($c_1 = 0$). If all the tablets did not dissolve (within the meaning of the test) a 100-tablet sample ($n_2 = 100$) was tested, and the batch was acceptable if two tablets ($c_2 = 2$) or less remained undissolved in the first and second sample of 150.

Let $P_a(p)$ = probability that a lot of quality p will be accepted. The lot will be accepted (*a*) if $c_1 = 0$ defectives appear in the first sample of $n_1 = 50$ *or* (*b*) if $c_2 = 2$ or less defectives appear in the first and second sample of 150.

The probability of (*a*) happening is $P_p(50,0)$, where we take

$$P_p(50, x) = \frac{(50p)^x e^{-50p}}{x!}$$

The probability of (*b*) happening consists of (*i*) the probability of 1 in 50 *and* 1 or less in 100 or (*ii*) the probability of 2 in 50 *and* 0 in 100.

These probabilities may be symbolized as

$$(i)\ P_p(50, 1) \sum_{x=0}^{1} P_p(100, x) \quad (ii)\ P_p(50, 2)\, P_p(100, 0)$$

Hence

$$P_a(p) = P_p(50, 0) + P_p(50, 1) \sum_{x=0}^{1} P_p(100, x) + P_p(50, 2)\, P_p(100, 0)$$

A work sheet now may be arranged, entries made

Received April 6, 1964, from the College of Pharmacy, University of Illinois at the Medical Center, Chicago.
Accepted for publication June 5, 1964.

TABLE I.—OPERATING CHARACTERISTIC CURVE FOR DOUBLE SAMPLING INSPECTION PLAN

$n_1 = 50,\ n_2 = 100,\ c_1 = 0,\ c_2 = 2$

$P_a(p) = P(50,0) + P(50,1)[P(100,0) + P(100,1)] + P(50,2)P(100,0)$

p	$P(50,0)$	$P(50,1)$	$P(50,2)$	$P(100,0)$	$P(100,1)$
.002	.905	.090	.005	.819	.164
.005	.779	.195	.024	.607	.303
.006	.741	.222	.033	.549	.329
.01	.607	.303	.076	.368	.368
.02	.368	.368	.184	.135	.271
.03	.223	.335	.251	.050	.149
.04	.135	.271	.271	.018	.074
.048	.091	.218	.261	.008	.040
.05	.082	.205	.257	.007	.034
.06	.050	.149	.224	.002	.015
.07	.030	.106	.185	.001	.006
.08	.018	.074	.146	.000	.003
.09	.011	.050	.112	.000	.001
.10	.007	.033	.085	.000	.000

$$
\begin{aligned}
P_a(.002) &= .905 + .090(.819 + .164) + .005(.819) = .998\\
P_a(.005) &= .779 + .195(.607 + .303) + .024(.607) = .971\\
P_a(.006) &= .741 + .222(.549 + .329) + .033(.549) = .954\\
P_a(.01) &= .607 + .303(.368 + .368) + .076(.368) = .858\\
P_a(.02) &= .368 + .368(.135 + .271) + .184(.135) = .542\\
P_a(.03) &= .223 + .335(.050 + .149) + .251(.050) = .302\\
P_a(.04) &= .135 + .271(.018 + .074) + .271(.018) = .165\\
P_a(.048) &= .091 + .218(.008 + .040) + .261(.008) = .103\\
P_a(.05) &= .082 + .205(.007 + .034) + .257(.007) = .092\\
P_a(.06) &= .050 + .149(.002 + .015) + .224(.002) = .053\\
P_a(.07) &= .030 + .106(.001 + .006) + .185(.001) = .031\\
P_a(.08) &= .018 + .074(.000 + .003) + .146(.000) = .018\\
P_a(.09) &= .011 + .050(.000 + .001) + .112(.000) = .011\\
P_a(.10) &= .007 + .033(.000 + .000) + .085(.000) = .007
\end{aligned}
$$

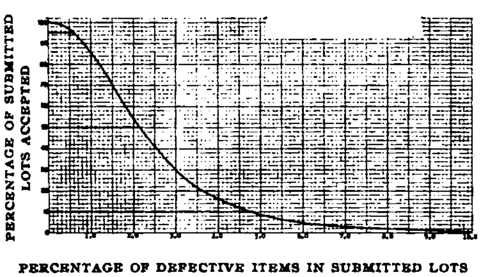

Fig. 1.—Operating characteristic curve for double sampling inspection plan. $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$. Sublot size 500.

from Molina's (2) tables for $p = 0$ to $p = .10$, and $P_a(p)$ computed.

Key features of our plan are (*a*) 95% of submitted lots accepted at about $p = .6\%$, (*b*) 10% of submitted lots accepted at about $p = 4.8\%$, and (*c*) 50–50 chance of acceptance at $p = 2.1\%$.

The slope of the tangent to the OC curve at and in a small neighborhood of $p = 0$ is of interest because a slope of zero implies no rejections. Obviously, $P_a(0) = 1.00$ for *any* plan, but the slope of the OC curve as $p \to 0$ indicates the power of the plan to detect small deviations from perfection in submitted lots. As a practical matter, one would generally prefer an OC curve which has essentially a zero slope for most values of p on the interval $0 \leq p \leq$ AQL. A plan whose OC curve approaches (0,1.00) with nonzero slope would operate to reject some lots of superior quality.

In the case of our double sampling plan, this property of slope of the OC curve near $p = 0$ may be studied as follows.

$$
\begin{aligned}
P_a(p) &= P(50,0) + P(50,1)\,[P(100,0) + P(100,1)] + P(50,2)P(100,0)\\
&= \frac{50!}{0!(50-0)!}\,p^0(1-p)^{50-0}\\
&\quad + \frac{50!}{1!(50-1)!}\,p^1(1-p)^{50-1}\\
&\quad \times \left[\frac{100!}{0!(100-0)!}\,p^0(1-p)^{100-0} + \frac{100!}{1!(100-1)!}\,p^1(1-p)^{100-1}\right]\\
&\quad + \frac{50!}{2!(50-2)!}\,p^2(1-p)^{50-2}\\
&\quad \times \frac{100!}{0!(100-0)!}\,p^0(1-p)^{100-0}\\
&= (1-p)^{50} + \frac{50!}{49!}\,p(1-p)^{49}\\
&\quad \times \left[(1-p)^{100} + \frac{100!}{99!}\,p(1-p)^{99}\right]\\
&\quad + \frac{50!}{2!48!}\,p^2(1-p)^{48}(1-p)^{100}\\
&= (1-p)^{50} + 50p(1-p)^{149}\\
&\quad + 5000p^2(1-p)^{148} + 1225\,p^2(1-p)^{148}\\
P_a'(p) &= -50(1-p)^{49} + 50[p^0(1-p)^{149}\\
&\quad - 149\,p(1-p)^{148}] + 5000[2p(1-p)^{148}\\
&\quad - 148\,p^2(1-p)^{147}] + 1225[2p(1-p)^{148}\\
&\quad - 148\,p^2(1-p)^{147}].
\end{aligned}
$$

If $p = 0$, $P_a'(p) = -50 + 50 = 0$.

This is an example of the case $c_1 = 0$, $c_2 \neq 0$, $p = 0$ gives $P_a'(p) = 0$. This case should not be taken as typical for all double sampling plans where $c_1 = 0$. There are double sampling plans for which $c_1 = 0$ and $P_a'(p) \neq 0$ as $p \to 0$.

Average Outgoing Quality (AOQ) Curve.—If all rejected lots are detailed, cleared of defectives, and all defectives replaced by good pieces, the equation for the AOQ curve becomes

$$\text{AOQ}(p) = P_a(p)p. \qquad \text{(Eq. 2)}$$

Derivation:

N = number of pieces in each lot
k lots at p
$NkP_a(p)$ accepted
$Nk[1 - P_a(p)]$ rejected
$NkP_a(p)p$ defective pieces accepted
$Nk[1 - P_a(p)]p$ defective pieces rejected

$$\text{AOQ}(p) = \frac{NkP_a(p)p + Nk[1 - P_a(p)](0)}{Nk} = P_a(p)p$$

The curve may be constructed from values already in the OC table.

If the rejected lots are detailed, cleared of defectives, and only the good pieces passed into stock, then

$$\text{AOQ}(p) = \frac{P_a(p)p}{1 - p[1 - P_a(p)]} \qquad \text{(Eq. 3)}$$

Derivation:

$$\frac{kN_p\,P_a(p)}{kN - kNp[1 - P_a(p)]} = \frac{P_a(p)p}{1 - p[1 - P_a(p)]}$$

This curve may be constructed similarly from values available in the OC table.

Table II.—Relationship Between Incoming Quality, Outgoing Quality, and AOQL

Assume all rejected lots are cleared of defectives and restored as 100% lots		If rejected lots are cleared of defectives but not restored	
$\text{AOQ}(p) = P_a(p)p$		$\text{AOQ}(p) = \frac{P_a(p)p}{1 - p[1 - P_a(p)]}$	
$n_1 = 50,\ n_2 = 100,\ c_1 = 0,\ c_2 = 2$			
AOQ(.002)	= .002	AOQ(.002)	= .002
(.005)	= .005	(.005)	= .005
(.006)	= .0057	(.006)	= .0057
(.01)	= .0086	(.01)	= .0086
(.02)	= .0108 ← AOQL	(.02)	= .0109 → AOQL
(.03)	= .0091	(.03)	= .0093
(.04)	= .0066	(.04)	= .0068
(.048)	= .0049	(.048)	= .0051
(.05)	= .0046	(.05)	= .0048
(.06)	= .0032	(.06)	= .0034
(.07)	= .0022	(.07)	= .0024
(.08)	= .0014	(.08)	= .0015
(.09)	= .0010	(.09)	= .0011
(.10)	= .0007	(.10)	= .0008

An important feature of these curves is the existence of a unique maximum point called the average outgoing quality limit (AOQL) and defined as the poorest average quality level which can occur in the long run after inspection, no matter what quality lots are submitted for inspection.

For our plan the curve of Eq. 2 is similar to the curve for Eq. 3. They are identical up to AOQL; at that point Eq. 3 exceeds Eq. 2. This relationship continues to the end of the curve. AOQL for Eq. 2 is 1.08% for $p \approx 2\%$; AOQL for Eq. 3 is 1.09% for $p \approx 2\%$. (See Table II and Figs. 2 and 3.)

Average Sample Number (ASN) Curve.—The expected number of pieces inspected to reach a decision regarding disposition of a lot will consist of

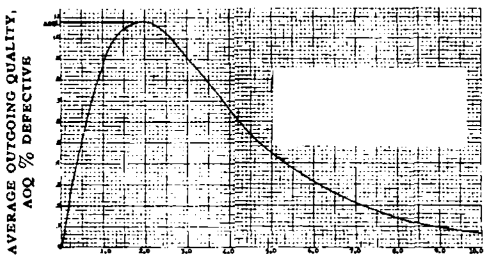

Fig. 2.—Relationship between incoming quality, outgoing quality, and AOQL. (Assume all rejected lots are cleared of defectives and restored as 100% lots.) $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$. AOQL = 1.08%. Sublot size 500.

three parts. (*a*) The average number required to accept the lot on the first sample, (*b*) the average number required to reject the lot on the first sample, (*c*) the average number required to reach a decision by virtue of inspecting a second sample.

If $P_{a_1}(p)$ = probability of accepting a lot of quality p on the first sample = $P_p(n_1, x \leq c_1)$ probability of c_1 or less in first n_1 observations from lot at level p.

If $P_{r_1}(p)$ = probability of rejecting a lot of quality p on first sample = $1 - P_p(n_1, x \leq c_2)$ probability of $c_2 + 1$ or more in first n_1 observations from lot at level p.

If $P_s(p)$ = probability of being required to take a second sample to reach a decision concerning disposition of the lot at level $p = P_p(n_1, x \leq c_2) - P_p(n_1, x \leq c_1)$ because

$$\sum_{x=0}^{c_1} P_p(n_1,x) + [1 - \sum_{x=0}^{c_2} P_p(n_1,x)] + P_s(p) = 1$$

Then

$$\text{ASN}(p) = n_1P_{a_1}(p) + n_1P_{r_1}(p) + (n_1 + n_2)P_s(p)$$

This supposition is that for each lot requiring a second sample, inspection of the second sample is carried to completion, even though an action decision is reached before $n_1 + n_2$ pieces have been inspected.

We shall show how this is constructed for our particular plan.

$$\text{ASN}(p) = 50[P_{a_1}(p) + P_{r_1}(p)] + 150P_s(p)$$

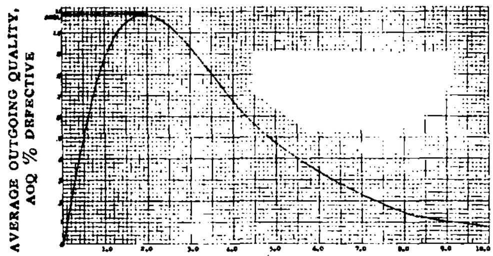

Fig. 3.—Relationship between incoming quality, outgoing quality, and AOQL. (If rejected lots are cleared of defectives but not restored.) $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$. AOQL = 1.09%. Sublot size 500.

Table III.—Average Sample Number Curve for Double Sampling

$n_1 = 50,\ n_2 = 100,\ c_1 = 0,\ c_2 = 2$

$\text{ASN}(p) = n_1[P_{a_1}(p) + P_{r_1}(p)] + (n_1 + n_2)P_s(p)$

p	$P_{a_1}(p)$	$P_{r_1}(p)$	$P_s(p)$	$n_1[P_{a_1}(p) + P_{r_1}(p)]$	$(n_1 + n_2)P_s(p)$	ASN
.002	.905	.000	.095	45.45	14.25	59.70
.005	.779	.002	.219	39.05	32.85	71.90
.006	.741	.004	.255	37.25	38.25	75.50
.01	.607	.014	.379	31.05	56.85	87.90
.02	.368	.080	.552	22.40	82.80	105.20
.03	.223	.191	.586	20.70	87.90	108.60
.04	.135	.323	.542	22.90	81.30	104.20
.048	.091	.430	.479	26.05	71.85	97.90
.05	.082	.456	.462	26.90	69.30	96.20
.06	.050	.577	.373	31.35	55.95	87.30
.07	.030	.679	.291	35.45	43.65	79.10
.08	.018	.762	.220	39.00	33.00	72.00
.09	.011	.826	.163	41.85	24.45	66.30
.10	.007	.875	.118	44.10	17.70	61.80

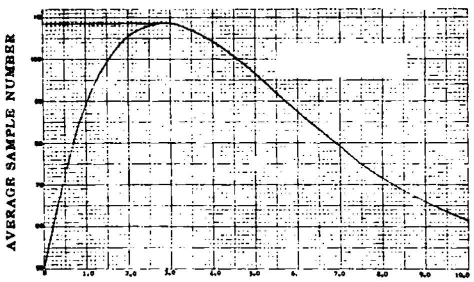

Fig. 4.—Average sample number curve for double sampling inspection plan. $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$.

Now

$$P_{a_1}(p) = P_p(n_1, x \le c_1) = P_p(50,0)$$

$$P_{r_1}(p) = 1 - P_p(n_1, x \le c_2) = 1 - \sum_{x=0}^{2} P_p(50,x)$$

$$P_s(p) = P_p(n_1, x \le c_2) - P_p(n_1, x \le c_1) = \sum_{x=0}^{2} P_p(50,x) - P_p(50,0)$$

Values of $P_{r_1}(p)$ and $P_s(p)$ may be approximated from Molina's tables for $p \le .10$, but the binomial is preferable for $p > .10$. Values of $P_{a_1}(p)$ are available from the OC table.

A plan should reach a decision early concerning when either material of very high quality or very poor quality is under inspection. Since first sample sizes in double sampling are always smaller than the corresponding fixed sample size in single sampling, double sampling achieves the objective of less inspection for both exceptionally high and exceptionally poor incoming quality. On the other hand, for material of intermediate quality the forcing of a second sample leads to more inspection than would be required by the corresponding single sampling plan. Therefore, the ASN curve as a function of continuously varying p must and does have a maximum value for some unique value of p.

We shall now show the approximate maximum ASN compared to the single sampling plan corresponding respectively to our plan.

The corresponding single sampling plan means here the plan that would be used for comparable incoming quality range and lot sizes. Strictly speaking, two sampling plans correspond with respect to their discriminatory power only when they have essentially congruent OC curves. Correspondence as used in this discussion only approximates this ideal.

ASN is 109 at $p \approx 3\%$ when $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$. Single sampling plan is $n = 75$, $c = 1$.

The ASN curves assume that all second samples are completely inspected, an assumption not likely to be realized in practice. The result of terminating the inspection on a second sample after a decision to reject is obtained will, of course, materially decrease the ASN values over the right half of the curve. (See Table III and Fig. 4.)

Total Amount of Inspection (TAI) Curve.—When acceptance procedures involve 100% detailing of all rejected lots, the question of what will be the expected total amount of inspection at each quality level arises.

The TAI figure is the sum of three components: (*a*) expected number of pieces inspected to accept on the first sample, (*b*) expected number of pieces inspected to accept on the second sample, (*c*) expected number of pieces inspected by virtue of detailing rejected lots. Thus, TAI is a function of two independent variables, p and N. If N = lot size, $P_s(p)$ = probability of taking second sample, and $P_2^*(p)$ = probability of acceptance on second sample. Hence

$$\text{TAI}(p,N) = n_1P_{a_1}(p) + (n_1 + n_2)P_s(p)P_{a_2}(p) + N[1 - P_s(p)P_{a_2}(p) - P_{a_1}(p)]$$

because

$$P_{a_1}(p) + P_s(p)P_{a_2}(p) + P_r(p) = 1.$$

For our plan $n_1 = 50$, $n_2 = 100$, $c_1 = 0$, $c_2 = 2$, and a lot size of 500 we have

$$\text{TAI}(p,500) = 50\,P_{a_1}(p) + 150\,P_s(p)P_{a_2}(p) + 500[1 - P_s(p)P_{a_2}(p) - P_{a_1}(p)]$$

Now

$$P_s(p)P_{a_2}(p) = P_a(p) - P_{a_1}(p)$$

so this and all other terms involved here are available from the OC table.

If the receiving staff does the detailing and uses the plan studied in this paper, it can expect to have

TABLE IV.—TOTAL AMOUNT OF INSPECTION CURVE

$n_1 = 50,\ n_2 = 100,\ c_1 = 0,\ c_2 = 2$

$N = 500$

$$\text{TAI}(p) = n_1 P_{a_1}(p) + (n_1 + n_2) P_s(p) P_{a_2}(p) + N[1 - P_s(p) P_{a_2}(p) - P_{a_1}(p)]$$

p	$P_{a_1}(p)$	$n_1 P_{a_1}(p)$	$P_s(p) P_{a_2}(p)$	$(n_1 + n_2) \cdot P_s(p) P_{a_2}(p)$	$N[1 - P_s(p) P_{a_2}(p) - P_{a_1}(p)]$	TAI(p)
.002	.905	45.25	.093	13.95	1.00	60.20
.005	.779	38.95	.192	28.80	14.50	82.25
.006	.741	37.05	.213	31.95	23.00	92.00
.01	.607	30.35	.251	37.65	71.00	139.00
.02	.368	18.40	.174	26.10	229.00	273.50
.03	.223	11.15	.079	11.85	349.00	372.00
.04	.135	6.75	.030	4.50	417.50	428.75
.048	.091	4.55	.012	1.80	448.50	454.85
.05	.082	4.10	.010	1.50	454.00	459.60
.06	.050	2.50	.003	.45	473.50	476.45
.07	.030	1.50	.001	.15	484.50	486.15
.08	.018	.90	.000	.00	491.00	491.90
.09	.011	.55	.000	.00	494.50	495.05
.10	.007	.35	.000	.00	496.50	496.85

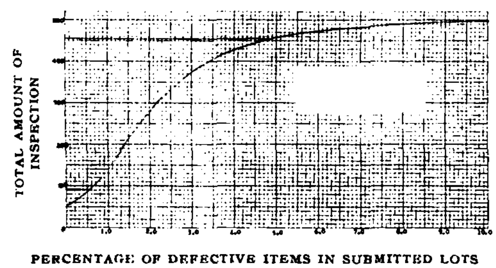

Fig. 5.—Total amount of inspection curve for double sampling inspection plan. $n_1 = 50$, $n = 100$, $c_1 = 0$, $c_2 = 2$. Lot size $N = 500$.

to inspect on the average 18% of every 500 piece lot that comes in at an AQL of .6%, and 91% of every 500 piece lot that comes in at a p_t of 4.8%. (See Table IV and Fig. 5.)

CONCLUSIONS

This paper has attempted to show how a given double sampling plan should be X-rayed to reveal its performance characteristics.

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Notes

Influence of Physostigmine and Neostigmine on the Responses of Goldfish Intestine to Acetylcholine

By THOMAS J. HALEY, G. COLVIN, and M. EFROS

The use of a microbath and electronic amplification of the contractions of goldfish intestine makes it possible to estimate acetylcholine in concentrations of 0.5 to 2.5 $\times 10^{-9}$ Gm. Addition of esterase inhibitors increases the sensitivity of the preparation, but it is not so sensitive as the leech muscle. Physostigmine and neostigmine also cause contractions of the goldfish intestine.

MANY MAMMALIAN intestinal preparations have been used to study the effects of biologically active substances, but Dreyer (1) was the first to describe the effects of acetylcholine and physostigmine on the fish intestine. Euler and Ostlund (2) extended these observations to include other materials, such as histamine, 5-hydroxytryptamine, and substance P. Gaddum and Szerb (3) showed that the intestine of the goldfish (*Carassius auratus*) could be used for such studies. Furthermore, the use of a microbath greatly increased the range of concentrations which could be investigated. However, Gaddum and Szerb (3) did not study the effects of physostigmine or neostigmine on the goldfish intestine. In view of the fact that such compounds generally increase the sensitivity of the intestine

Received June 29, 1964, from the Laboratory of Nuclear Medicine and Radiation Biology, Department of Biophysics and Nuclear Medicine, School of Medicine, University of California at Los Angeles, Los Angeles.
Accepted for publication August 18, 1964.
These studies were supported by contract AT(04-1)GEN-12 between the Atomic Energy Commission and the University of California.