Rework and Postponement: A comparison of bottling strategies

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Abstract

This paper presents the results of a case study in a batch production facility for biological vaccines. The problem considered is that of finding the best bottling strategy for produced batches. A batch can be bottled directly after production, after positive intermediate test results, or after positive final test results. Strategies that start the bottling process quickly after production, have the advantages of a low capacity requirement for production tanks and of a small throughput time if all test results are positive. However, a production batch can only be reworked as long as it has not been bottled. So fast bottling reduces the possibilities for rework and therefore reduces the production yield. We present performance measures for comparing the different strategies and derive closed-form expressions for them. We illustrate the results obtained for the considered case.

Keywords: process industry, rework, yield uncertainty, case study.

1 Introduction

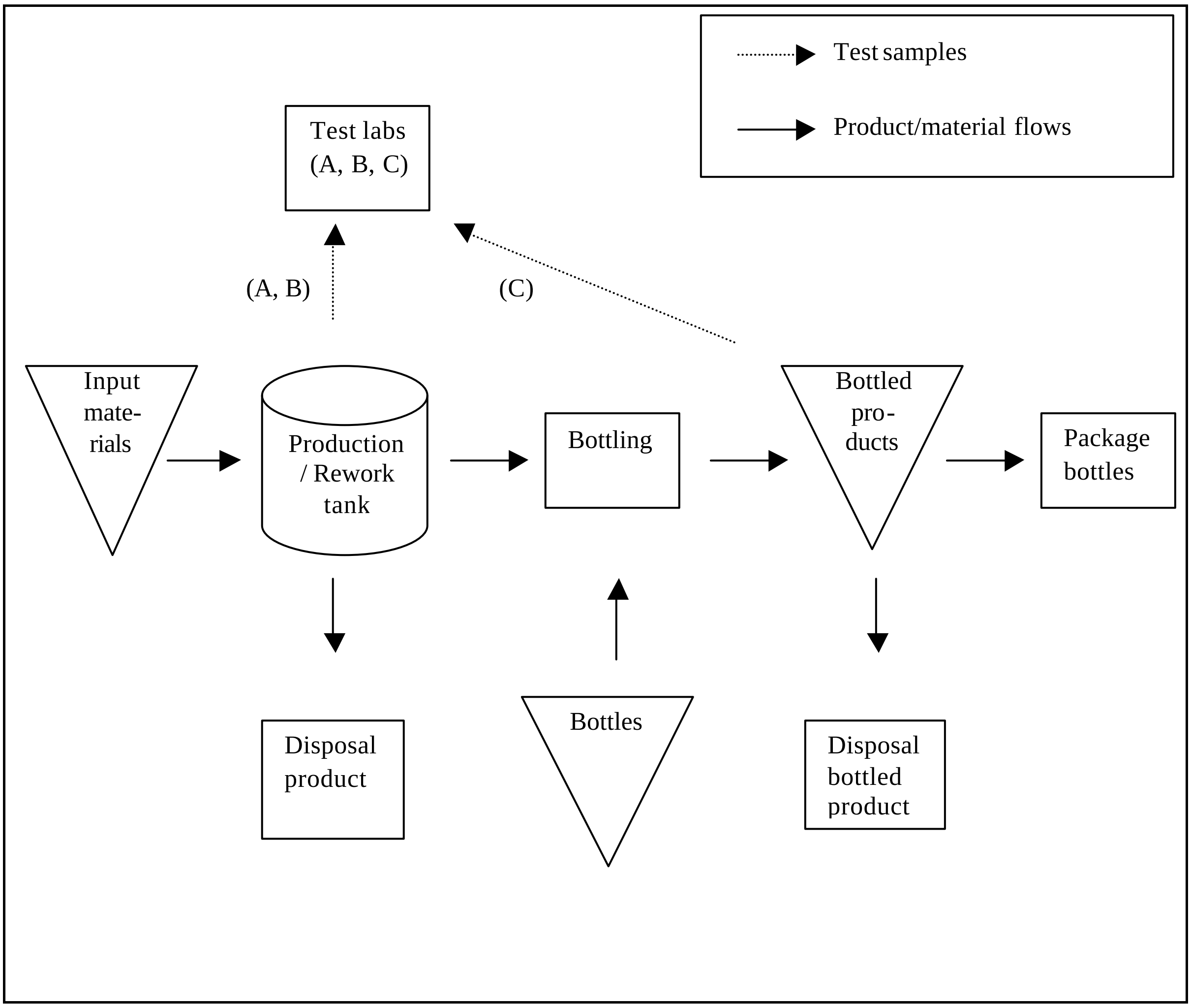
A standard (implicit) assumption in the quality control literature is that products are not tested and processed simultaneously. That is, if the quality of a semi-finished product is tested, then further processing is postponed until test results are available. However, stopping the processing of a product during testing had two important disadvantages. First, it increases the total processing time, which is especially undesirable for perishable (e.g. milk based) products. Second, either special storage facilities for products-in-process are required, or a loss of production capacity results because products cannot leave the production line during testing.

These disadvantages are relatively more important in situations with long test times (compared to process times) and reliable processes (high probabilities of passing tests). In such situations, it may therefore be better to continue processing a product while (a sample of) it is being tested. On the other hand, this may reduce the possibilities for correcting actions in case of a positive (a test is failed) test result, leading to more scrap and higher production costs.

This paper deals with the above-mentioned trade-off for a facility that produces (biological) vaccines. Before discussing the trade-off for this specific company in detail, we first sketch the company background and the production process.

The company is an important worldwide player with several production facilities. The production facility that we consider in this paper produces mainly biological vaccines. The production process consists of three steps: (batch) production, bottling, and packaging into boxes. Tests are required after production and after bottling. After production, two samples of the produced batch are sent to different test laboratories. Both tests start directly and are hence performed simultaneously. The first sample is tested for sterility. The results of this 'batch sterility' test (A) are known after 2 weeks. The second sample is used to test whether the product is of sufficient quality. This second test is actually a collection of tests, but they can be considered together as one 'quality test' (B). This quality test consists of two phases (B1 and B2) that have to be performed sequentially and require 6 and 3 weeks, respectively. After bottling, a sample of bottles is tested for sterility. The results of this 'bottle sterility' test (C) are known after 2 weeks. See Figure 1 for a graphical illustration of the production system.

Figure 1. Schematic representation of the production system.



The problem that we consider is that of finding the best bottling strategy for each type of product. A batch can be bottled directly after completion of production/rework (i.e. after 0 weeks), after a positive result for test A (i.e. after 2 weeks), after positive results for tests A and B1 (i.e. after 6 weeks), or after positive results for tests A, B1, and B2 (i.e. after 9 weeks).

The main advantage of bottling directly after production is that batches do not require extra 'tank time' for storage. This is important, since the tank capacity is a bottleneck in the production process. An additional advantage of bottling after 0, 2, or 6 instead of 9 weeks, is that tests B and C can be performed simultaneously, which reduces the throughput time by two weeks (assuming that all test results are positive). However, fast bottling limits rework options. A negative result for test A, B1, or B2 does not necessarily imply that a batch has to be disposed of. In many cases, such a batch can be reworked as long as it has not been bottled. Since rework takes less time and is cheaper than production, it is an interesting alternative. So fast bottling reduces rework possibilities, which may lead to higher production costs, disposal costs, and purchase costs for input materials and bottles.

It is clear from the above arguments that, ideally, one would like to remove a batch from a production tank directly/shortly after it is completed, but bottle that batch at a later time. That strategy could be realised using special storage tanks. Although the company has considered such storage tanks in the past, they are currently not available. Therefore, we will not include them in this analysis. We remark however, that the analysis can easily be extended for situations with storage tanks, and that such an extended analysis could be useful for making future investment decisions about storage tanks.

Combining the above alternatives results in 4 possible strategies:

1. Bottle a batch directly after production has finished.
2. Bottle a produced/reworked batch if the result of test A is positive.
3. Bottle a produced/reworked batch if the results of test A and B1 are positive.
4. Bottle a produced/reworked batch if the results of test A, B1, and B2 are positive.

For all these strategies, the following rules apply.

- If the production/rework of a batch is completed, start tests A and B.
- If a batch is bottled, start test C.
- If there is a negative test result and rework is possible, stop all tests and start rework.
- If there is a negative test result and rework is not possible, stop all tests, dispose of the (bottled) batch, and start the production of a new batch.
- If all test results are positive, package the bottles.

From the above, it is clear that the strategies differ in required tank time, in throughput time, and in cost. Therefore the following performance measures for comparing the different bottling strategies are used:

- expected total cost per serviceable (passed all tests) batch,
- expected tank time (in weeks) per serviceable batch, and
- expected throughput time (in weeks) per serviceable batch.

In the remainder of this paper, we will derive mathematical expressions for these three performance measures for all four strategies. In Section 2, the system is described mathematically. We list the assumptions, discuss which costs are relevant, and introduce notations. In Section 3, we actually derive the above-mentioned expressions. In Section 4, we illustrate the use of these expressions using real-life (though rescaled) data. We end with conclusions and directions for future research in Section 5.

2 System description

We make the following assumptions:

As1 The production time, rework time, and test times are constant.

As2 The bottling time, packaging time, and waiting time before a production tank is available and production can start, are negligible compared to the test times.

As3 The results of sterility tests A and C are (pair-wise) independent of the results of quality tests B1 and B2 (but there is dependence between A and C, and between B1 and B2.)

As4 There is a certain maximum number of times that a batch is reworked.

As5 The probability that a reworked batch fails a test is independent of the number of times the batch has been reworked before. That probability can be different, however, for a new produced batch.

As6 The probability that a reworked batch, which fails a certain test, can be reworked is independent of the number of times the batch has been reworked before. That probability can be different, however, for a new produced batch.

As7 A batch that fails test C cannot be reworked.

The assumption (part of As2) of negligible waiting times is the most debatable. It is needed to keep the analysis of throughput times tractable. Without this assumption, all products would have to be analysed simultaneously, requiring a complex stochastic (queuing) analysis. Under the assumption of a negligible waiting time, the expected throughput time per serviceable batch can be determined separately for each product and deterministically. Of course, once the bottling strategy for each product has been fixed and the tank time per serviceable batch for each product has been calculated, a stochastic (queuing) analysis can be used afterwards to calculate the number of tanks which ensures a negligible (compared to the test times) waiting time. We will not perform such a complex analysis is this paper, but we will illustrate in Section 4 how a lower bound for the number of tanks can easily be derived from the calculated tank times. We remark that the assumption of a negligible waiting time does not influence the expected total cost and the expected tank time per serviceable batch.

All other assumptions are realistic. The production time, rework time, and test times are indeed almost constant (As1). In fact, the test times are the same for each product: 2 weeks for tests A and C, 6 weeks for test B1, and 3 weeks for test B2. Bottling and packaging takes hours, whereas producing, reworking, and testing takes weeks (As2). The results of tests A, B, and C are indeed independent (As3). A batch is never reworked more than 2 or 3 times (As4). The number of times that a batch has already been reworked hardly influences the probability that tests are passed (As5) or that the batch can again be reworked if some test is not passed (As6). A batch that fails test C can never be reworked, since it is already bottled (As7).

As mentioned before, Assumption As2 allows us to analyse each product separately. In the remainder of this model, we will therefore focus on one specific product. The goal is to determine the expected total cost per serviceable (passed all tests) batch, the expected required production tank capacities, and the expected throughput time. The following operational costs are included: production cost, rework cost, bottling cost, costs for purchasing input materials and bottles, costs for disposing of unbottled and bottled batches, and costs for testing. With respect to the costs for testing, we assume that these occur when a test is started. So when a test is stopped before the result is known, because the vaccine fails another test that is performed simultaneously, testing costs are not reduced. The throughput time is defined as the length of the time interval from the decision to produce a batch until a serviceable batch is obtained.

The notations that we will use are listed in Table 1. Since tests A and B1 start if and only if the production/rework of a batch is finished, the costs for tests A and B1 are included in the production cost and in the rework cost. Similar, the cost for test C is included in the bottling cost. In this way the number of cost parameters is reduced.

Table 1. Notations.

Time lengths	
T_P	Production time (per batch)
T_R	Rework time (per batch)
(Conditional) Probabilities that a (new) produced batch or a reworked batch passes a test	
p_A	Probability that a produced batch passes test A
p_{B1}	Probability that a produced batch passes test B1
p_{B2}	Probability that a produced batch passes test B2 if it passed test B1
p_C	Probability that a produced batch passes test C if it passed test A
r_A	Probability that a reworked batch passes test A
r_{B1}	Probability that a reworked batch passes test B1
r_{B2}	Probability that a reworked batch passes test B2 if it passed test B1
r_C	Probability that a reworked batch passes test C if it passed test A
Probability that a (new) produced batch or a reworked batch, if it fails a test and is not yet bottled, can be reworked	
q_A	Probability that a produced batch which fails test A can be reworked
q_{B1}	Probability that a produced batch which fails test B1 can be reworked
q_{B2}	Probability that a produced batch which fails test B2 can be reworked
s_A	Probability that a reworked batch which fails test A can (again) be reworked
s_{B1}	Probability that a reworked batch which fails test B1 can (again) be reworked
s_{B2}	Probability that a reworked batch which fails test B2 can (again) be reworked
Costs (per batch)	
c_p	Production cost, including purchase cost of input materials and costs of tests A + B1
c_r	Rework cost, including purchase cost of extra materials and costs of tests A + B1
c_b	Bottling cost, including purchase cost of bottles and cost of test C
c_{B2}	Test B2 cost
c_{du}	Net (minus possible revenues) disposal cost unbottled
c_{db}	Net (minus possible revenues) disposal cost bottled
Performance measures	
P_1	Expected total cost per serviceable (passed all tests) batch
P_2	Expected tank time per serviceable batch (in weeks)
P_3	Expected throughput time per serviceable batch (in weeks)
Other	
R	Maximum number of times that a batch is reworked ($R \in \{1,2,\ldots\}$)

3 Derivation of the performance measures

In this section, we derive expressions for the three performance measures P_1, P_2, P_3. These expressions are valid for all four strategies. We first introduce some additional (strategy-dependent) notations in Table 2.

Table 2. Additional notations (strategy-dependent).

Probabilities for *production*	
$\Pr_{p,s}$	Probability that a produced batch is *serviceable* (passes all tests)
$\Pr_{p,r}$	Probability that a produced batch fails some test, is still unbottled, and can be *reworked*
$\Pr_{p,du}$	Probability that a produced batch fails some test, is still *unbottled*, but can not be reworked and has to be *disposed* of
$\Pr_{p,db}$	Probability that a produced batch fails some test, is already *bottled*, and hence has to be *disposed* of
Probabilities for *rework*	
$\Pr_{r,s}$	Probability that a reworked batch is *serviceable* (passes all tests)
$\Pr_{r,r}$	Probability that a reworked batch fails some test, is still unbottled, and can be *reworked* **Remark**: If the batch has already been reworked R times, it has to be disposed of!
$\Pr_{r,du}$	Probability that a reworked batch fails some test, is still *unbottled*, but can not be reworked and has to be *disposed* of
$\Pr_{r,db}$	Probability that a reworked batch fails some test, is already *bottled*, and hence has to be *disposed* of
Expectations for *production*	
$E_{p,c}$	Expected total *costs* until a produced batch is serviceable, disposed of, or ready for rework (costs during and after rework, if a batch is reworked, are not included)
$E_{p,tk}$	Expected *tank* time until a produced batch is serviceable, disposed of, or ready for rework (tank time during and after rework, if a batch is reworked, is not included)
$E_{p,tm}$	Expected *time* until a produced batch is serviceable, disposed of, or ready for rework
Expectations for *rework*	
$E_{r,c}$	Expected total *costs* until a reworked batch is serviceable, disposed of, or ready for another round of rework (costs during and after another round of rework, if a batch is reworked again, are not included) **Remark**: Disposal cost for an unbottled batch that can be reworked, but is not because it has already been reworked R times, is excluded from this variable (not from the analysis, of course!)
$E_{r,tk}$	Expected *tank* time until a reworked batch is serviceable, disposed of, or ready for another round of rework (tank time during and after another round of rework, if a batch is reworked again, is not included)
$E_{r,tm}$	Expected *time* until a reworked batch is serviceable, disposed of, or ready for another round of rework

The derivations of the three expressions for the performance measures are similar. We will present the derivation for P_1, the expected total cost per serviceable (passed all tests) batch, as an example.

To that end, we focus on an arbitrary batch from the moment that it enters the system until the moment it leaves the system, i.e., from the moment that production starts until the moment that the batch is either (serviceable and) packaged or disposed of. The probability that production directly results in a serviceable batch is $\Pr_{p,s}$. The probability that the batch is serviceable after reworking it n, $n = 1,2,\ldots$, times is $\Pr_{p,r}(\Pr_{r,r})^{n-1}\Pr_{r,s}$. Since a batch is reworked at most R times, the total probability that production results in a serviceable batch is $\Pr_{p,s} + \sum_{n=1}^{R}[\Pr_{p,r}(\Pr_{r,r})^{n-1}\Pr_{r,s}]$. The average number of batches needed to obtain one serviceable batch is the reciproce of this probability. For instance, if the total probability that production results in a serviceable batch is 0.50 then, on average, 1/0.50 = 2 batches have to be produced/reworked in order to get one serviceable batch. The probability that a batch is reworked for the n-th time ($n = 1,2,\ldots,R$) is $\Pr_{p,r}(\Pr_{r,r})^{n-1}$, and hence the total expected costs for one produced batch are $E_{p,c} + \sum_{n=1}^{R}[\Pr_{p,r}(\Pr_{r,r})^{n-1}E_{r,c}] + \Pr_{p,r}(\Pr_{r,r})^{R}c_{du}$. The last term represents the disposal cost if the batch is unbottled and can be reworked, but is disposed of because it has already been reworked R times (this cost is not included in $E_{r,c}$, see the notations in Table 2). This gives

$$P_1 = \frac{E_{p,c} + \sum_{n=1}^{R}[\Pr_{p,r}(\Pr_{r,r})^{n-1}E_{r,c}] + \Pr_{p,r}(\Pr_{r,r})^{R}c_{du}}{\Pr_{p,s} + \sum_{n=1}^{R}[\Pr_{p,r}(\Pr_{r,r})^{n-1}\Pr_{r,s}]}$$
$$= \frac{(1-\Pr_{r,r})E_{p,c} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})E_{r,c} + (1-\Pr_{r,r})\Pr_{p,r}(\Pr_{r,r})^{R}c_{du}}{(1-\Pr_{r,r})\Pr_{p,s} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})\Pr_{r,s}}. \quad (1)$$

Similar derivations give

$$P_2 = \frac{(1-\Pr_{r,r})E_{p,tk} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})E_{r,tk}}{(1-\Pr_{r,r})\Pr_{p,s} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})\Pr_{r,s}},$$
$$P_3 = \frac{(1-\Pr_{r,r})E_{p,tm} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})E_{r,tm}}{(1-\Pr_{r,r})\Pr_{p,s} + \Pr_{p,r}(1-(\Pr_{r,r})^{R})\Pr_{r,s}}. \quad (2)$$

What remains to be determined, are the probabilities and expectations in the above expressions for each strategy separately. This is done in Section 3.1 for Strategy 1 and in Appendix A for the other three strategies.

3.1 Strategy 1: Bottle a batch directly after production is completed.

Since bottled batches cannot be reworked, we have $\Pr_{p,r} = 0$. So, for this strategy, the rework probabilities and expectations are not relevant. The production probabilities and expectations can be determined using the 'scenario-table' below. That table has a separate row for each possible scenario, i.e. a combination of test results until some test is failed or all tests are passed. The scenarios are listed in ascending order of duration, based on the availability of test results: A and C (2 weeks), B1 (6 weeks), B2 (9 weeks). The columns give the corresponding probability, duration, costs (excluding disposal costs), tank time, and whether or not the batch is bottled at the end of a scenario. We remark that disposal costs are excluded from this table to be consistent with similar scenario-tables for the other three strategies in Appendix A. If disposal costs would be included in the tables in Appendix A, then the rows for rejected unbottled batches would have to be duplicated into one for a reworkable and one for a non-reworkable batch. For readability, disposal costs are therefore excluded from the scenario-tables. Of course, we do include the disposal cost in the cost expressions and hence in the cost performance measure.

Table 3. Different scenarios under strategy 1.

PRODUCTION	Probability	Duration	Costs (excl. disposal)	Tank time	Bott-led?
Fail A or C	$1 - p_A p_C$	$T_P + 2$	$c_p + c_b$	T_P	Yes
Pass A and C, fail B1	$p_A (1 - p_{B1}) p_C$	$T_P + 6$	$c_p + c_b$	T_P	Yes
Pass A, C, and B1; fail B2	$p_A p_{B1} (1 - p_{B2}) p_C$	$T_P + 9$	$c_p + c_b + c_{B2}$	T_P	Yes
Pass all	$p_A p_{B1} p_{B2} p_C$	$T_P + 9$	$c_p + c_b + c_{B2}$	T_P	Yes

Using the above table, and the fact that a batch is disposed of if not all tests are passed, we get

$$\Pr_{p,s} = p_A p_{B1} p_{B2} p_C,$$
$$\Pr_{p,r} = 0,$$
$$\Pr_{p,du} = 0,$$
$$\Pr_{p,db} = 1 - p_A p_{B1} p_{B2} p_C,$$
$$E_{p,c} = c_p + c_b + c_{B2} p_A p_{B1} p_C + c_{db}(1 - p_A p_{B1} p_{B2} p_C),$$
$$E_{p,tk} = T_P,$$
$$E_{p,tm} = T_P + 2 + 4 p_A p_C + 3 p_A p_{B1} p_C. \qquad (3)$$

Combining (1), (2), and (3) gives

$$P_1 = \frac{E_{p,c}}{\Pr_{p,s}} = \frac{c_p + c_b + c_{B2} p_A p_{B1} p_C + c_{db}(1 - p_A p_{B1} p_{B2} p_C)}{p_A p_{B1} p_{B2} p_C},$$
$$P_2 = \frac{E_{p,tk}}{\Pr_{p,s}} = \frac{T_P}{p_A p_{B1} p_{B2} p_C},$$
$$P_3 = \frac{E_{p,tm}}{\Pr_{p,s}} = \frac{T_P + 2 + 4 p_A p_C + 3 p_A p_{B1} p_C}{p_A p_{B1} p_{B2} p_C}.$$

In the next section, we will estimate all model parameters and calculate the performance measures (for all 4 strategies) using real-life (though rescaled) data.

4 Data and results

Production (and rework) of biological vaccines takes place in two types of tanks, small and large. Annual demand for a product determines which type of tank is used. Table 1 gives the tank type for each product (A, B, …, O) and the estimated number of serviceable batches that are needed to satisfy annual demand. Table 1 also gives the process times per batch and the rescaled costs per batch. Table 2 gives the additional input that is needed to apply our model.

Table 4. Tank type, number of batches per year, process times, and costs.

Vac-cine	Tank (volume per batch)	Batches per year	Process times (in days) Production $7T_P$	Rework $7T_R$	Rescaled costs Production c_p	Rework c_r	Bottling c_b	Test B2 c_{B2}	Disposal unbottled c_{du}	Disposal bottled c_{db}
A	Large	17	5	4	14	6	8	3	0.6	0.6
B	Large	15	5	4	18	6	8	3	0.6	0.6
C	Small	3	5	4	23	7	9	3	0.6	0.6
D	Large	6	10	9	86	13	6	3	0.6	0.6
E	Small	2	10	9	38	9	7	3	0.6	0.6
F	Large	2	5	4	187	22	8	3	0.6	0.6
G	Large	13	13	12	79	12	9	3	0.6	0.6
H	Large	2	4	3	23	6	9	3	0.6	0.6
I	Large	19	13	12	100	14	6	3	0.6	0.6
J	Small	3	5	4	21	7	9	3	0.6	0.6
K	Large	2	4	3	119	16	10	3	0.6	0.6
L	Small	2	7	6	66	10	12	3	0.6	0.6
M	Small	2	4	3	50	9	12	3	0.6	0.6
N	Large	6	5	4	39	9	18	3	0.6	0.6
O	Small	3	5	4	21	6	7	3	0.6	0.6

Table 5. Test and rework probabilities.

Vac-cine	Probability that a produced batch passes a test p_A	p_{B1}	p_{B2}	p_C	Probability that a reworked batch passes a test r_A	r_{B1}	r_{B2}	r_C	Probability that a batch can be reworked if it fails a test $q_A = s_A$	$q_{B1} = s_{B1}$	$q_{B2} = s_{B2}$
A	0.993	0.980	0.980	0.990	0.997	0.990	0.990	0.995	0	0.9	0.8
B	0.999	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0	0.9	0.8
C	0.999	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0	0.9	0.8
D	0.993	0.990	0.990	0.990	0.997	0.995	0.995	0.995	0	0.9	0.8
E	0.979	0.975	0.975	0.970	0.990	0.988	0.988	0.985	0	0.9	0.8
F	0.979	0.965	0.965	0.970	0.990	0.983	0.983	0.985	0	0.9	0.8
G	0.979	0.975	0.975	0.970	0.990	0.988	0.988	0.985	0	0.9	0.8
H	0.979	0.980	0.980	0.970	0.990	0.990	0.990	0.985	0	0.9	0.8
I	0.979	0.980	0.980	0.970	0.990	0.990	0.990	0.985	0	0.9	0.8
J	0.999	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0	0.9	0.8
K	0.999	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0	0.9	0.8
L	0.979	0.935	0.935	0.970	0.990	0.968	0.968	0.985	0	0.9	0.8
M	0.979	0.965	0.965	0.970	0.990	0.983	0.983	0.985	0	0.9	0.8
N	0.979	0.965	0.965	0.970	0.990	0.983	0.983	0.985	0	0.9	0.8
O	0.999	0.998	0.998	0.998	0.999	0.999	0.999	0.999	0	0.9	0.8

We calculate the performance measures P_1-P_3 for strategies 1-4 for all products A-O. The complete results for $R = 2$ are given in Appendix B. Other values of R produce similar results. This is explained by the fact that the production and rework processes are reliable (high probabilities for passing tests), and hence it is seldom required to rework a product more than once.

A first important conclusion from the results in Appendix B is that postponing the bottling leads to a cost reduction for all products. This is caused by the preference of rework over production, due to the shorter (one day) process time, the much lower process cost, and the higher probabilities of passing tests.

A second conclusion is that the cost reduction from postponing the bottling is larger for products with high failure probabilities. This is illustrated by the results for products B and L, which are given below. These products have been selected because they have the lowest (1%) and highest (18%) probability $(1 - p_A p_{B1} p_{B2} p_C)$, respectively, for not passing all tests.

Table 6. Results for product B ($R = 2$).

Product B	Strategy 1	2	3	4
Cost P_1	29.2	29.2	29.2	29.1
Tank time P_2	0.7	2.7	6.8	9.8
Throughput time P_3	9.8	9.8	9.8	11.8

Table 7. Results for product L ($R = 2$).

Product L	Strategy 1	2	3	4
Cost P_1	97.3	97.0	91.9	87.8
Tank time P_2	1.2	3.6	8.3	11.5
Throughput time P_3	11.4	11.5	11.5	13.6

The results for product L also illustrate a third conclusion: postponing the bottling until test A is passed (i.e., going from strategy 1 to strategy 2) leads to a relatively small cost reduction compared to those for postponing until test B1 is passed (i.e., going from strategy 2 to strategy 3) and further postponing until test B2 is passed (i.e., going from strategy 3 to strategy 4). This is explained by the fact that a product which fails test A can never be reworked, whereas products that fail tests B1 or B2 can be reworked in most cases. So, postponing the bottling until test A is passed only reduces the bottling cost, whereas further postponements also reduce process costs.

A fourth conclusion, illustrated by the results for products B and L, is that the throughput time is almost the same under strategies 1, 2, and 3, but two weeks more under strategy 4. The almost identical throughput times under strategies 1, 2, and 3 result from equal test times and similar process times (difference of one day) for production and rework. The throughput time under strategy 4 is two weeks more, since test C cannot be performed simultaneously with other tests.

Based on the above findings, we propose to either use a mixture of strategy 1 for some products and strategy 3 for the other products ('1-or-3-policy'), or use a mixture of strategies 1 and 4 ('1-or-4-policy'). A 1-or-3-policy should be chosen if throughput times are important, and a 1-or-4-policy should be chosen otherwise. For both types of policies, we determine a series of 'cost versus tank time efficient' solutions (combinations of strategies for separate products) as follows. We start with strategy 1 for all products, and then change to strategy 3(4) for one product at a time, always choosing that product with the highest ratio of cost reduction and tank time increase. As an example, for the 1-or-3-policy and product L (see Table 7), this ratio is (97.3-91.9)/(8.3-1.2).

Since there are two types of tanks (small and large), the above-proposed method is applied separately for the two corresponding sets of products. The results are represented graphically in Figures 2 and 3. The total cost per year and the required number of tanks that are given in those figures for each solution are calculated as follows. Determine the cost per year for each product by multiplying the cost per batch (Appendix B) with the number of batches per year (Table 4). Add those costs per year for all products to obtain the total cost per year. Determine the tank time (in weeks) per year for each product by multiplying the tank time per batch (Appendix B) with the number of batches per year (Table 4). Transform to tank time in years by dividing with 46 (tanks are estimated to be available for production or rework during 46 weeks of a year). Add the tank times in years for all products to obtain the required number of tanks. We illustrate these calculations for the following solution for large tanks: apply strategy 4 for products L, M, and E, and strategy 1 for products C, J, and O. The total cost per year is $87.8\times 2+69.4\times 2+51.1\times 2+35.2\times 3+33.2\times 3+31.2\times 3=715.5$. The required number of tanks is $(11.5\times 2+10.5\times 2+11.3\times 2+0.7\times 3+0.7\times 3+0.7\times 3)/46=1.59$. We remark that the required number of tanks resulting from this analysis (1.59 for the above example) is actually a lower bound for the required number of tanks. Some spare tank capacity is needed to ensure small waiting times before the processing of a batch can start. See Section 2.

It is important to remark that the required number of tanks, given in Figures 2 and 3 for each proposed solution, is just enough to ensure that the yearly production covers the yearly-expected demand (number of batches given in Table 4) for each product. In practise, some spare capacity is needed to protect against variations in demand and variations in production yield. A stochastic (queuing) analysis could be used to determine the required spare capacity. See also the discussion in Section 2.

Figure 2. Annual cost and required number of large tanks under a 1-or-3-policy or 1-or-4-policy, starting with strategy 1 for all products (left hand side) and changing to strategy 3(4) for one product at a time.

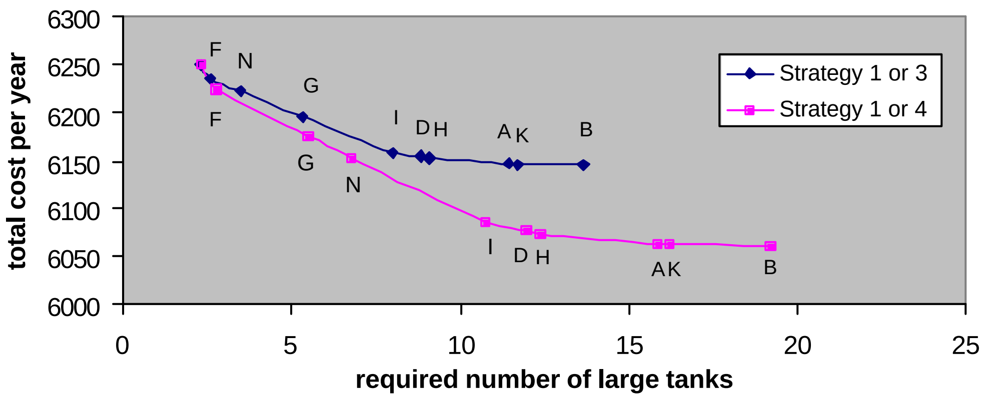
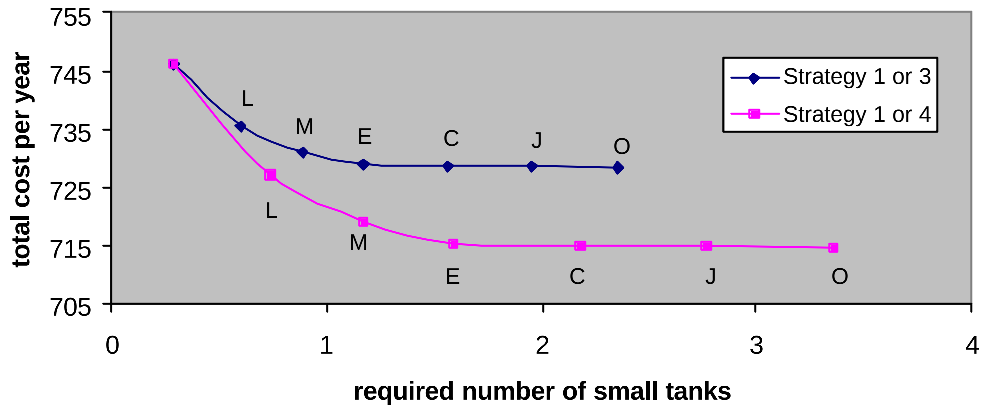


Figure 3. Annual cost and required number of small tanks under a 1-or-3-policy or 1-or-4-policy, starting with strategy 1 for all products (left hand side) and changing to strategy 3(4) for one product at a time.



5 Conclusions

We have analysed a production facility for multiple biological vaccines. The problem considered was that of choosing the bottling strategy for each vaccine. The first possible strategy is to bottle a batch as soon as production finishes. Three alternative strategies postpone bottling and leave a finished batch in the production tank until (some or all) test results are known. We developed a model that can be used to compare these strategies for each vaccine separately, based on the assumption that the production capacity is sufficient to ensure small waiting times before a production tank becomes available. For all four strategies, closed-form expressions were derived for three performance measures: the expected total cost per serviceable (passed all tests) batch, the expected tank time (in weeks) per serviceable batch, and the expected throughput time (in weeks) per serviceable batch.

After collecting data, the three performance measures for each of the four strategies were calculated for all vaccines. Based on the results, we proposed combinations of bottling strategies for the different vaccines. For each of those combinations, we indicated the total cost per year and the required number of tanks (no spare capacity) in a graph. This graph aids the decision maker in trading off cost and capacity. Of course, it is important to keep in mind that there should be enough spare capacity to ensure small waiting times (as assumed in our model). In a follow-up study, stochastic (queuing) analysis could be used to determine the required spare capacity for a given combination of strategies.

The model and analysis that we presented can be adapted and applied to other multi-stage, multi-product production systems with variable yield, rework options, and several time consuming tests. They provide valuable insight into the potentials of rework, and aid a decision maker in trading of cost, capacity requirement, and throughput time.

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A Derivation of probabilities and expectations for strategies 2, 3, 4

We use the notations in Tables 1 and 2. The derivations are similar to those for strategy 1 in Section 3.1.

Strategy 2: Bottle a produced/reworked batch if the result of test A is positive (after 2 weeks so that the test C result is known after 4 weeks).

The order of the test results is: A (2 weeks), C (4 weeks), B1 (6 weeks), B2 (9 weeks).

Table 3. Different scenarios under strategy 1.

PRODUCTION	Probability	Duration	Costs (excl. disposal)	Tank time	Bott-led?
Fail A	$1-p_A$	T_P+2	c_p	T_P+2	No
Pass A; fail C	$p_A(1-p_C)$	T_P+4	c_p+c_b	T_P+2	Yes
Pass A and C; fail B1	$p_A(1-p_{B1})p_C$	T_P+6	c_p+c_b	T_P+2	Yes
Pass A, B1 and C; fail B2	$p_A p_{B1}(1-p_{B2})p_C$	T_P+9	$c_p+c_b+c_{B2}$	T_P+2	Yes
Pass all	$p_A p_{B1} p_{B2} p_C$	T_P+9	$c_p+c_b+c_{B2}$	T_P+2	Yes

$$\Pr_{p,s} = p_A p_{B1} p_{B2} p_C,$$
$$\Pr_{p,r} = (1-p_A)q_A,$$
$$\Pr_{p,du} = (1-p_A)(1-q_A),$$
$$\Pr_{p,db} = p_A(1-p_C) + p_A(1-p_{B1})p_C + p_A p_{B1}(1-p_{B2})p_C,$$
$$E_{p,c} = c_p + c_b p_A + c_{B2} p_A p_{B1} p_C + c_{du}\Pr_{p,du} + c_{db}\Pr_{p,db},$$
$$E_{p,tk} = T_P + 2,$$
$$E_{p,tm} = T_P + 2 + 2p_A + 2p_A p_C + 3p_A p_{B1} p_C.$$

Similarly, we get

$$\Pr_{r,s} = r_A r_{B1} r_{B2} r_C,$$
$$\Pr_{r,r} = (1-r_A)s_A,$$
$$\Pr_{r,du} = (1-r_A)(1-s_A),$$
$$\Pr_{r,db} = r_A(1-r_C) + r_A(1-r_{B1})r_C + r_A r_{B1}(1-r_{B2})r_C,$$
$$E_{r,c} = c_p + c_b r_A + c_{B2} r_A r_{B1} r_C + c_{du}\Pr_{r,du} + c_{db}\Pr_{r,db},$$
$$E_{r,tk} = T_R + 2,$$
$$E_{r,tm} = T_R + 2 + 2r_A + 2r_A r_C + 3r_A r_{B1} r_C.$$

Strategy 3: Bottle a produced/reworked batch if the results of test A and B1 are positive (after 6 weeks so that the test C result is known after 8 weeks).

The order of the test results is: A (2 weeks), B1 (6 weeks), C (8 weeks), B2 (9 weeks).

PRODUCTION	Probability	Duration	Costs (excl. disposal)	Tank time	Bott-led?
Fail A	$1-p_A$	T_P+2	c_p	T_P+2	No
Pass A; fail B1	$p_A(1-p_{B1})$	T_P+6	c_p	T_P+6	No
Pass A and B1; fail C	$p_A p_{B1}(1-p_C)$	T_P+8	$c_p+c_b+c_{B2}$	T_P+6	Yes
Pass A, B1 and C; fail B2	$p_A p_{B1}(1-p_{B2})p_C$	T_P+9	$c_p+c_b+c_{B2}$	T_P+6	Yes
Pass all	$p_A p_{B1} p_{B2} p_C$	T_P+9	$c_p+c_b+c_{B2}$	T_P+6	Yes

$$\Pr_{p,s}=p_A p_{B1} p_{B2} p_C,$$
$$\Pr_{p,r}=(1-p_A)q_A+p_A(1-p_{B1})q_{B1},$$
$$\Pr_{p,du}=(1-p_A)(1-q_A)+p_A(1-p_{B1})(1-q_{B1}),$$
$$\Pr_{p,db}=p_A p_{B1}(1-p_C)+p_A p_{B1}(1-p_{B2})p_C,$$
$$E_{p,c}=c_p+c_b p_A p_{B1}+c_{B2} p_A p_{B1}+c_{du}\Pr_{p,du}+c_{db}\Pr_{p,db},$$
$$E_{p,tk}=T_P+2+4p_A,$$
$$E_{p,tm}=T_P+2+4p_A+2p_A p_{B1}+p_A p_{B1} p_C.$$

Similarly, we get

$$\Pr_{r,s}=r_A r_{B1} r_{B2} r_C,$$
$$\Pr_{r,r}=(1-r_A)s_A+r_A(1-r_{B1})s_{B1},$$
$$\Pr_{r,du}=(1-r_A)(1-s_A)+r_A(1-r_{B1})(1-s_{B1}),$$
$$\Pr_{r,db}=r_A r_{B1}(1-r_C)+r_A r_{B1}(1-r_{B2})r_C,$$
$$E_{r,c}=c_r+c_b r_A r_{B1}+c_{B2} r_A r_{B1}+c_{du}\Pr_{r,du}+c_{db}\Pr_{r,db},$$
$$E_{r,tk}=T_R+2+4r_A,$$
$$E_{r,tm}=T_R+2+4r_A+2r_A r_{B1}+r_A r_{B1} r_C.$$

Strategy 4: Bottle a produced/reworked batch if the results of test A, B1, and B2 are positive (after 9 weeks so that the test C result is known after 11 weeks).

The order of the test results is: A (2 weeks), B1 (6 weeks), B2 (9 weeks), C (11 weeks).

PRODUCTION	Probability	Duration	Costs (excl. disposal)	Tank time	Bott-led?
Fail A	$1-p_A$	T_P+2	c_p	T_P+2	No
Pass A; fail B1	$p_A(1-p_{B1})$	T_P+6	c_p	T_P+6	No
Pass A and B1; fail B2	$p_A p_{B1}(1-p_{B2})$	T_P+9	c_p+c_{B2}	T_P+9	No
Pass A, B1 and B2; fail C	$p_A p_{B1} p_{B2}(1-p_C)$	T_P+11	$c_p+c_b+c_{B2}$	T_P+9	Yes
Pass all	$p_A p_{B1} p_{B2} p_C$	T_P+11	$c_p+c_b+c_{B2}$	T_P+9	Yes

$$\Pr_{p,s} = p_A p_{B1} p_{B2} p_C,$$
$$\Pr_{p,r} = (1-p_A)q_A + p_A(1-p_{B1})q_{B1} + p_A p_{B1}(1-p_{B2})q_{B2},$$
$$\Pr_{p,du} = (1-p_A)(1-q_A) + p_A(1-p_{B1})(1-q_{B1}) + p_A p_{B1}(1-p_{B2})(1-q_{B2}),$$
$$\Pr_{p,db} = p_A p_{B1} p_{B2}(1-p_C),$$
$$E_{p,c} = c_p + c_b p_A p_{B1} p_{B2} + c_{B2} p_A p_{B1} + c_{du} \Pr_{p,du} + c_{db} \Pr_{p,db},$$
$$E_{p,tk} = T_P + 2 + 4p_A + 3p_A p_{B1},$$
$$E_{p,tm} = T_P + 2 + 4p_A + 3p_A p_{B1} + 2p_A p_{B1} p_{B2}.$$

Similarly, we get

$$\Pr_{r,s} = r_A r_{B1} r_{B2} r_C,$$
$$\Pr_{r,r} = (1-r_A)s_A + r_A(1-r_{B1})s_{B1} + r_A r_{B1}(1-r_{B2})s_{B2},$$
$$\Pr_{r,du} = (1-r_A)(1-s_A) + r_A(1-r_{B1})(1-s_{B1}) + r_A r_{B1}(1-r_{B2})(1-s_{B2}),$$
$$\Pr_{r,db} = r_A r_{B1} r_{B2}(1-r_C),$$
$$E_{r,c} = c_p + c_b r_A r_{B1} r_{B2} + c_{B2} r_A r_{B1} + c_{du} \Pr_{r,du} + c_{db} \Pr_{r,db},$$
$$E_{r,tk} = T_P + 2 + 4r_A + 3r_A r_{B1},$$
$$E_{r,tm} = T_P + 2 + 4r_A + 3r_A r_{B1} + 2r_A r_{B1} r_{B2}.$$

B Performance measures for all strategies and all products ($R = 2$)

Product A	Strategy 1	2	3	4
Cost P_1	26.4	26.3	26.0	25.7
Tank time P_2	0.8	2.9	7.1	10.2
Throughput time P_3	10.1	10.1	10.2	12.2

Product B	Strategy 1	2	3	4
Cost P_1	29.2	29.2	29.2	29.1
Tank time P_2	0.7	2.7	6.8	9.8
Throughput time P_3	9.8	9.8	9.8	11.8

Product C	Strategy 1	2	3	4
Cost P_1	35.2	35.2	35.2	35.1
Tank time P_2	0.7	2.7	6.8	9.8
Throughput time P_3	9.8	9.8	9.8	11.8

Product D	Strategy 1	2	3	4
Cost P_1	98.5	98.5	97.8	97.1
Tank time P_2	1.5	3.6	7.7	10.7
Throughput time P_3	10.7	10.7	10.7	12.8

Product E	Strategy 1	2	3	4
Cost P_1	53.0	52.8	52.0	51.1
Tank time P_2	1.6	3.8	8.1	11.3
Throughput time P_3	11.1	11.1	11.3	13.3

Product F	Strategy 1	2	3	4
Cost P_1	223.7	223.5	217.2	211.8
Tank time P_2	0.8	3.1	7.5	10.7
Throughput time P_3	10.5	10.5	10.6	12.7

Product G	Strategy 1	2	3	4
Cost P_1	100.6	100.4	98.5	96.8
Tank time P_2	2.1	4.3	8.6	11.8
Throughput time P_3	11.6	11.6	11.7	13.8

Product H	Strategy 1	2	3	4
Cost P_1	38.2	38.0	37.5	37.0
Tank time P_2	0.6	2.8	7.1	10.3
Throughput time P_3	10.0	10.1	10.2	12.3

Product I	Strategy 1	2	3	4
Cost P_1	119.3	119.2	117.4	115.8
Tank time P_2	2.0	4.2	8.5	11.7
Throughput time P_3	11.5	11.5	11.6	13.7

Product J	Strategy 1	2	3	4
Cost P_1	33.2	33.2	33.2	33.1
Tank time P_2	0.7	2.7	6.8	9.8
Throughput time P_3	9.8	9.8	9.8	11.8

Product **K**	Strategy 1	2	3	4
Cost P_1	132.9	132.9	132.7	132.5
Tank time P_2	0.6	2.6	6.6	9.6
Throughput time P_3	9.6	9.6	9.6	11.6

Product **L**	Strategy 1	2	3	4
Cost P_1	97.3	97.0	91.9	87.8
Tank time P_2	1.2	3.6	8.3	11.5
Throughput time P_3	11.4	11.5	11.5	13.6

Product **M**	Strategy 1	2	3	4
Cost P_1	73.3	73.0	71.1	69.4
Tank time P_2	0.6	2.9	7.3	10.5
Throughput time P_3	10.3	10.4	10.5	12.6

Product **N**	Strategy 1	2	3	4
Cost P_1	67.6	67.2	65.5	63.8
Tank time P_2	0.8	3.1	7.5	10.7
Throughput time P_3	10.5	10.5	10.6	12.7

Product **O**	Strategy 1	2	3	4
Cost P_1	31.2	31.2	31.2	31.1
Tank time P_2	0.7	2.7	6.8	9.8
Throughput time P_3	9.8	9.8	9.8	11.8