Sampling Plan for Microbial Testing of Natural Origin Products

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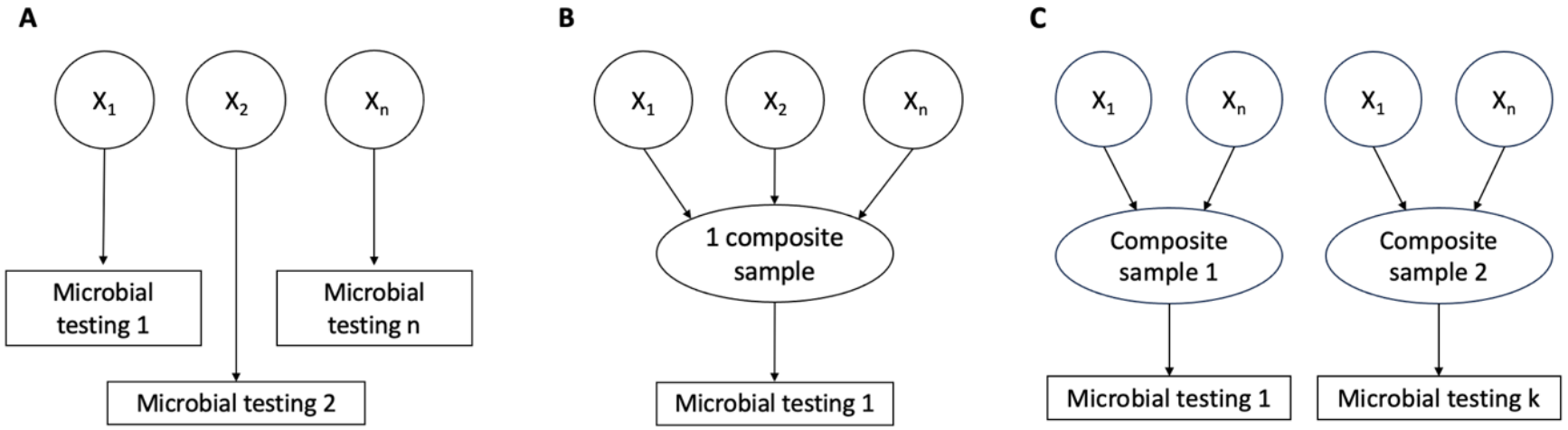
Microbial Testing of Natural Origin products

- Testing for bacterial contamination in products of natural origin used in the pharmaceutical industry is essential to ensure the quality and safety of products.
  - Pre-gelatinized starch is a natural origin product that serves as a binder in pharmaceutical manufacturing to improve the cohesion of the powder mixture.
- When a shipment of this natural origin product is received by a manufacturing site, microbial testing of this product before formal acceptance/use is done based on a set of guidelines (e.g. WHO Technical Report Series TRS 929 – Annex 4).
- To unambiguously check the quality of interest, one may inspect every item in the lot, however, such an approach is costly and often unnecessary for ensuring product quality.

Individual vs Composite Sampling

Sampling schemes for a single shipment (lot) with N bags (units)



A. Individual Sampling/Testing, i.e. test each individual bag, WHO* r-plan with $n = 1.5\sqrt{N}$

B. and C. Composite testing:

- Group the samples into k composite samples
- Assume either perfect or imperfect mixing, based on Dirichlet distribution**
- Test the composite samples

B. Composite Sampling I, i.e. WHO* n-plan with $n = 1 + \sqrt{N}$

C. Composite Sampling II, i.e. WHO* p-plan with k composite samples and n bags per composite sample. $k = 0.4\sqrt{N}$

*TRS 929 - Annex 4: WHO guidelines for sampling of pharmaceutical products and related materials. WHO Technical Report Series, No.929, 2005.

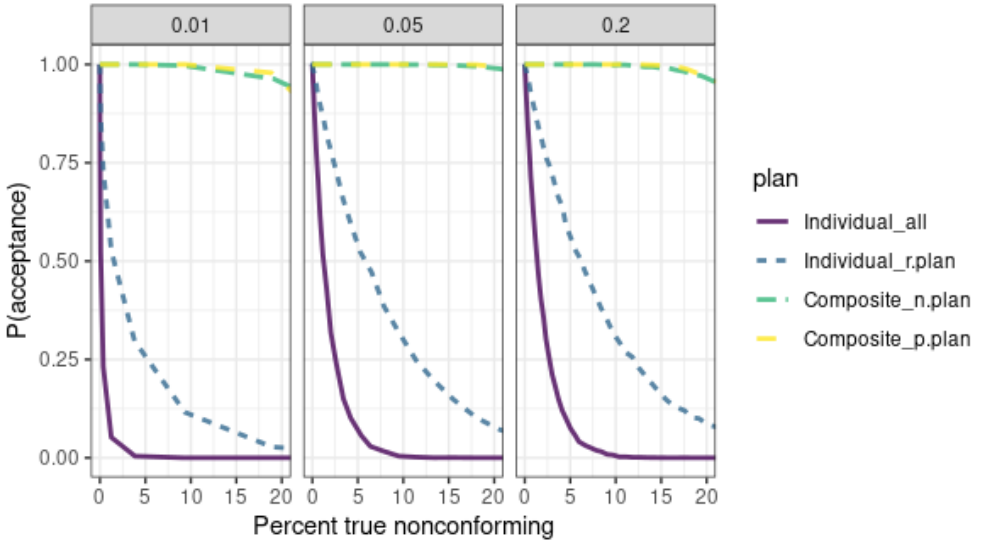
**Santos-Fernández, E., Govindaraju, K., & Jones, G. (2015). Variables sampling plans using composite samples for food quality assurance. Food Control, 50, 530–538. hkps://doi.org/10.1016/J.FOODCONT.2014.09.041.

Results

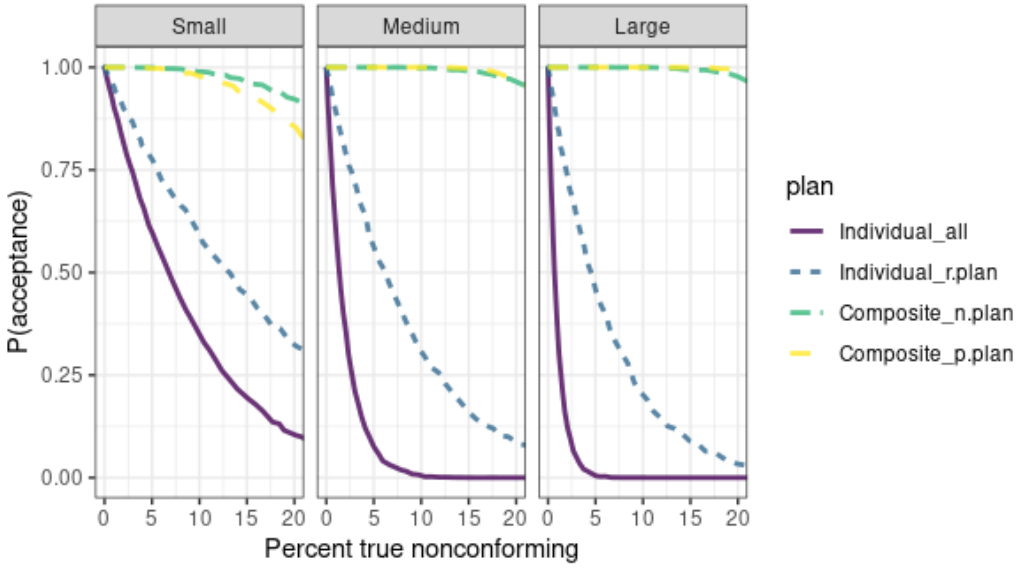
- Probability of accepting the lot using the **microbiological limit of 100 CFU/g**
- Comparison of the OC curves for different sampling plans
  - different between-bag variability (equivalent to CV of approx. 2%, 12%, 49%),
  - different lot sizes,
  - different within-bag variability, mixing quality

Lot	Number of bags	plan	Sample Size
Small	10	n-plan	1 (5)
		r-plan	5
		p-plan	2 (5)
Medium	50	n-plan	1 (9)
		r-plan	11
		p-plan	3 (16)
Large	100	n-plan	1 (11)
		r-plan	15
		p-plan	4 (25)

1. Effect of different between bag SD



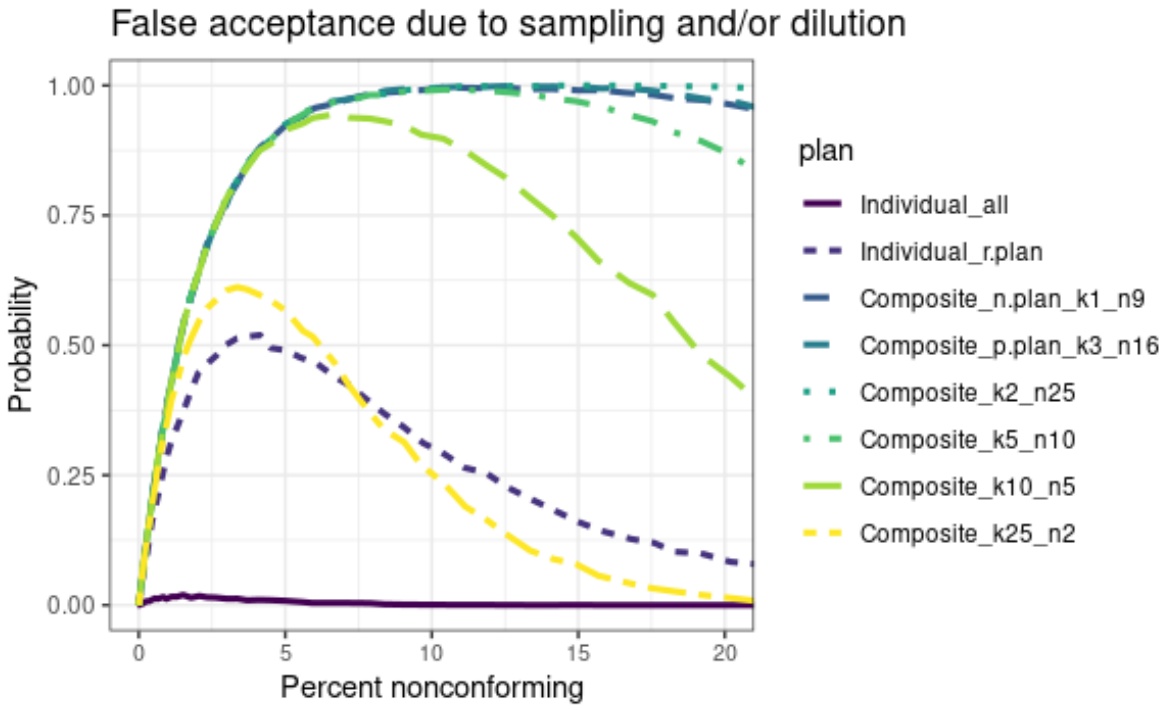
2. Effect of different lot size

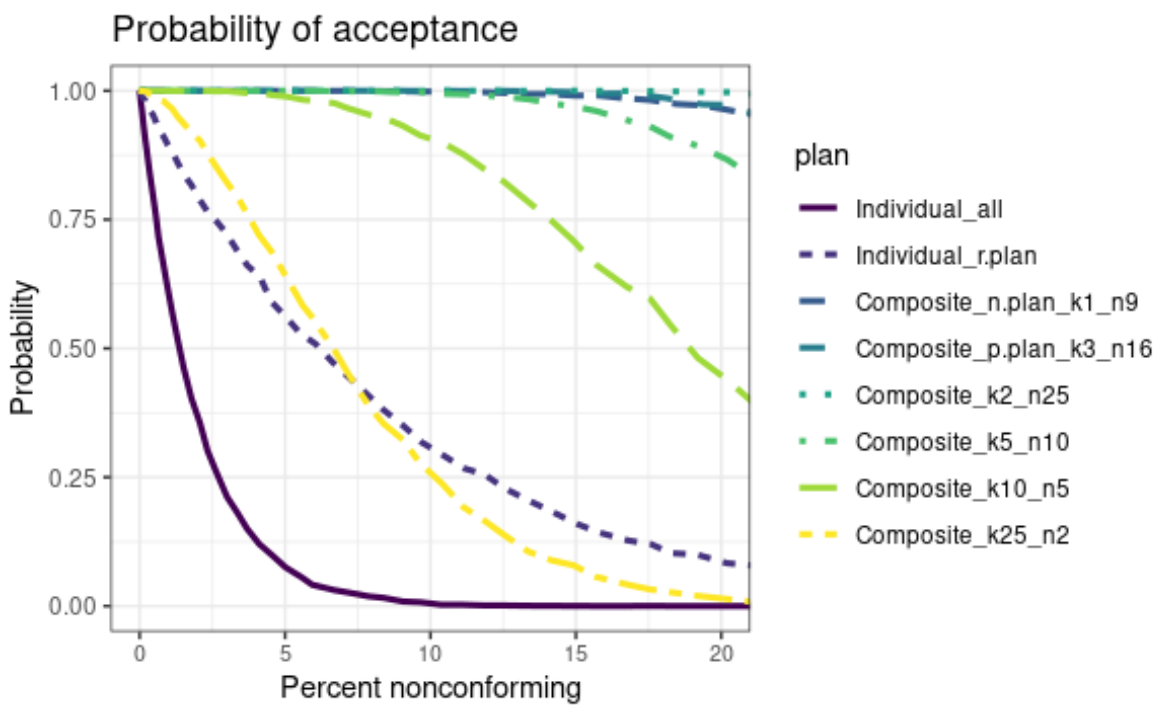


Plot 1: Nsim=5000; Within-bags SD = 0.01; Lot-size = 50

Plot 2: Nsim=5000; Between-bags SD = 0.2; Within-bags SD = 0.01

Results





- Comparison of the OC curves for different sampling plans, assuming medium lot size.
- Medium lot (N=50), r-plan sample size = 11
- Composite sampling dilution effect: Probability of accepting the composite sample with at least one individual item outside the specification limit

Nsim=5000; Between-bags SD = 0.2; Within-bags SD = 0.01;
Lot-size = 50

Conclusion

- Utilizing composite samples for testing is efficient to reduce workload.
- Potential savings might not outweigh dilution risk.
- Decision to opt for composite samples or individual samples depends on heterogeneity of the lot, the effectiveness of the mixing, and the acceptable levels of consumer risk.
- For this application, mixing process is not as important as within-lot heterogeneity.

- Recommendation:
  - Use of WHO r-plan (individual sampling) given possible heterogeneity
  - Properties close to other plans, i.e. sampling all bags and compositing.
  - Usage of composite samples not recommended in this case. Although for known suppliers having less variable lots, compositing might be acceptable.

Thank you

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If you have more questions, please contact:
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