

---

# Implementation of statistical innovation in a pharmaceutical company - it can be done!

*Kaspar Rufibach*

*Merck KGaA, Darmstadt*

*BBS webinar 19th March 2025*



**I will tell a story.**

**I have not been part of that story.**

**Story is partly discussed in  
Rufibach et al. (2025).**

**I acknowledge Roche  
statistics team + collaborators.**

**Imagine the following situation:**

**Pharma company runs two very large  
very expensive Phase 3 trials in  
key indication.**

**Treatment policy strategy for ICE  
of treatment discontinuation.**

**Estimation via MMRM. Uses data as it  
comes, inference valid under MAR.**

**MAR not plausible for this estimand.**

**What was needed?**

**Primary estimand and estimator aligned.**

**Statistical theory  $\Rightarrow$  conditional mean  
imputation + jackknife.**

**(validated) Software  $\Rightarrow$  `rbmi` package.**

**Output templates.**

**Stats team made the company change  
primary analysis in these trials.**

**No statistical method.**

**No validated implementation.**

**No reporting templates.**

**No regulator had ever seen it.**

**Estimated effect smaller than with MMRM.**

**BUT THEY DID IT.**

**HOW?**





**Invention: new method.**

**Commercialization: scaled-up  
implementation of invention.**

**Innovation = invention × commercialization.**



## Implementation of Statistical Innovation in a Pharmaceutical Company

Kaspar Rufibach<sup>a</sup>, Marcel Wolbers<sup>a</sup> , Jenny Devenport<sup>b</sup> , Godwin Yung<sup>c</sup> , Chris Harbron<sup>d</sup>, Alun Bedding<sup>d</sup>, Zhiyue Huang<sup>e</sup> , Ray Lin<sup>c</sup>, Herbert Pang<sup>c</sup>, Daniel Sabanés Bové<sup>f</sup>, and Jianmei Wang<sup>d</sup>

<sup>a</sup>Methods, Collaboration, and Outreach Group, Product Development Data Sciences (MCO), Hoffmann-La Roche Ltd, Basel, Switzerland; <sup>b</sup>Product Development Data Sciences, Hoffmann-La Roche, Basel, Switzerland; <sup>c</sup>MCO, Genentech, South San Francisco, California, US; <sup>d</sup>MCO, Hoffmann-La Roche Products Ltd, Welwyn, UK; <sup>e</sup>MCO, Hoffmann-La Roche, Shanghai, China; <sup>f</sup>Data Science Acceleration, Product Development Data Sciences, Hoffmann-La Roche Ltd, Basel Switzerland

### ABSTRACT

Innovation, defined as the successful implementation at scale of a new invention, is key for continued success of the drug development enterprise. In this article we focus on statistical innovation in the pharmaceutical industry. We discuss both components, *invention* and implementation at scale, typically called *commercialization*, of innovation for statistical methods. These concepts are illustrated using three examples that we successfully implemented in our company. We summarize factors that foster or hinder invention and commercialization. A discussion of the mindset we consider supportive of innovation and how organizational leaders and professional organizations can generate an environment that fosters innovation concludes the article.

### ARTICLE HISTORY

Received November 2023  
Accepted March 2024

### KEYWORDS

Innovation; Invention;  
Collaboration;  
Commercialization; Statistics

# Rufibach et al. (2025)

# Potential hurdles for commercialization

- **Insufficient knowledge.**
- **Lack of case studies.**
- **Lack of user friendly software.**
- **Regulatory position.**
- **Company-internal buy-in.**
- **Inertia.**
- **Statistician's mindset.**

*Yes, but have you thought about the assumptions, and this and that and blablabla. Ah, and by the way your proposal is great!*

Rufibach et al. (2025): details & how to overcome hurdles.

# Some success factors to innovate

- **Entrepreneurial spirit:**
  - Experts who are capable and can invest resources at their leisure.
  - Ownership, accountability.
  - Trust, reputation, credibility, network.
- **Organizational culture:** Accept failures without compromising on quality of work.
- **Specialized capabilities & investment.**
- **Statistical engineering.**
- **External collaboration.**
- **Designated project leadership.**
- **Timelines / urgency.**
- **Tools to facilitate adoption.**
- **Collaborations:**
  - Internally in other functions.
  - Industry, regulators, academics.

# What statisticians do we need for innovation?

# Curiosity!



# What statisticians do we need for innovation?

- Solid experience in drug development.
- **Invention:**
  - Broad methodological competence in statistics relevant to drug development.
  - Curiosity.
  - Park statistician's mindset of emphasizing everything that could go wrong.
  - Trust and credibility.
  - Collaborative: other methodologists, wherever they sit.
  - Remain connected to the drug development business.
- **Commercialization:**
  - Self-starter and pro-active.
  - Collaborative: Statistical engineering; statisticians working on projects; cross-functional molecule teams; senior management; regulators.
  - Persistence.
  - Modesty and teamwork. Sharing credit with collaborators who commercialize an invention is essential.

Hire for both!

**Innovation = invention × commercialization.**

**Hurdles and how to overcome them.**

**Curiosity! And a few other things.**

**It can be done!**

**Thank you for your attention.**

**[kaspar.rufibach@merckgroup.com](mailto:kaspar.rufibach@merckgroup.com)**

**Slides can be downloaded on  
[www.kasparrufibach.ch](http://www.kasparrufibach.ch)**



# References

- ▶ Rufibach, K., Wolbers, M., Devenport, J., Yung, G., Harbron, C., Bedding, A., Huang, Z., Lin, R., Pang, H., Sabanés Bové, D. and Wang, J. (2025). Implementation of statistical innovation in a pharmaceutical company. *Statistics in Biopharmaceutical Research* **17** 113–124.

**R version and packages used to generate these slides:**

R version: R version 4.4.2 (2024-10-31 ucrt)

Base packages: stats / graphics / grDevices / utils / datasets / methods / base

Other packages:

This document was generated on 2025-03-19 at 14:28:53.