



CMC Statistics Network Europe – EFSPi SIG

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CMC Statistical Network
Europe

“We are CMC Statisticians, working in Europe for pharmaceutical companies and CROs active in R&D, and we seek to collaborate and exchange in any precompetitive topic of our field . “

This is what we want ...

1

... facilitate technical exchange in any precompetitive topic of our field.

2

... be seen as point of contact for EMA etc. for CMC stats related guidelines, solicit and corroborate feedback from members.

3

... encourage discussion on current good practice for design, computing, evaluation, and reporting in the CMC space.

4

... create a platform for the community of European CMC statisticians.



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CMC Statistics Network Europe ...so far



- Chair Kevin.R.Lief@gsk.com
- Affiliated to EFSPi as a special interest group
- 80+ members, from 25+ organisations
- Still welcoming members: Do not have to be a member of EFSPi or PSI to join
- SIG website: <https://www.psiweb.org/sigs-special-interest-groups/cmc-statistical-network-europe>



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Purpose

Chemistry, Manufacturing and Control Statisticians, working in Europe for pharmaceutical companies and CROs active in R&D, and we seek to collaborate and exchange in any precompetitive topic of our field.

Formed as a SIG in 2024, we seek to:

1. Arrange webinars to share various technical, novel and existing approaches.
2. Provide a forum for CMC Statisticians in Europe to comment on guidelines from regulatory agencies.



Since NCS2024

- Listen & learn focus group meeting of the EMA Quality Innovation Group
- EFSPi regulatory workshops (2025 oral presentation and 2026 poster)
- Creating a CMC Stats Community of Practice
- Webinars
- Working groups



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EMA Quality Innovation Group

Listen & learn focus group meeting of the EMA Quality Innovation Group

Executive Summary

Statistical approaches to develop data-driven prior knowledge into a Platform

Beate Presser PhD, Boehringer-Ingelheim (Head of CMC Statistics Biologics)

Kevin Lief, GlaxoSmithKline (Director, CMC Statistics)

Affiliations: European Federation of Statisticians in the Pharmaceutical Industry (EFPSI)
Steering Committee CMC Statistics Network Europe (CSNE)

SPECIAL INTEREST GROUP



- Prior knowledge in development can enhance new project development and resulting product understanding, greater process confidence and increase quality.
- Statistical methodologies such as frequentist, machine learning, and Bayesian can be used to integrate prior knowledge.
- Statistical methodologies can be provided by data-driven models which can be mathematically validated and their quality checked.
- Data-driven approaches to prior knowledge can lead to more efficient drug product development and faster access to medical products for patients.

EFSPI regulatory workshops

EFSPI regulatory workshops (2025 oral presentation and 2026 poster)

"How can we strengthen statisticians' impact in CMC related ICH guidelines?"

Special focus on ICH M13b concerning dissolution profiles

Thomas Hoffelder, PhD, Boehringer-Ingelheim

Beate Presser, PhD, Boehringer-Ingelheim

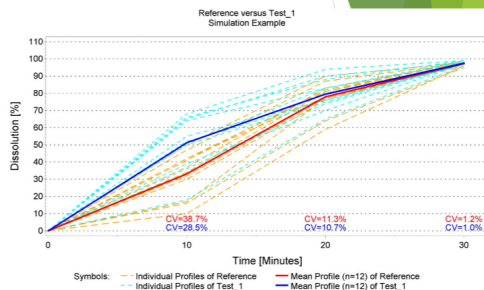
Christian Schmid, PhD, Roche

Affiliations: European Federation of Statisticians in the Pharmaceutical Industry (EFSPi)
CMC Statistics Network Europe (CSNE)



Disso profiles Intro - relationship to BE

- Context: post-approval changes (PACs)
- surrogates for BE studies: disso profile study successful --> BE study not necessary
- ICH E6: "avoid unnecessary burden on participants" --> Need for **sufficiently powered** disso profile studies to **avoid unnecessary** BE studies.



CMC - Chemistry, Manufacturing, and Controls

CMC Statisticians in the Pharmaceutical Industry

Focus Areas:

- Manufacturing Control
- Process Development
- Regulatory Registration

Core Contributions:

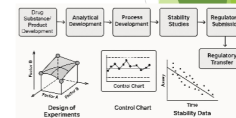
Provide a data-driven foundation ensuring:

- High Quality and Consistency of manufactured drugs to be safe and effective
- Stability and safety compliance through strict quality controls
- Efficient and cost-effective product development

Despite their critical contributions, CMC statisticians hold a limited role in guidelines and regulatory interactions.

Key Guidelines:

- Q1: Stability
- Q2/Q14: Analytical Method Validation
- Q6: Specifications
- Q8: Pharmaceutical Development
- Q9: Quality Risk Management
- ...



Questions

- (ICH E6, M-CERSI workshop 2019, EFSPi RSW 2019) versus (ICH M13b) How to solve these conflicts? Suggestion: Establishing a working group of **statisticians** to develop a guidance/white paper/... on the **statistical aspects** of dissolution profile studies. Do you agree?
- Do you agree that statistical methodologies could also be part of the QIG discussions? E.g. stability modelling...
- What opportunities do you see for CMC statisticians to contribute more consistently to guideline development, such as ICH Q6? How do you view the role of statisticians in justifying specifications?
- Could you envision a constructive role for EFSPi - CSNE in contributing to guideline discussions, and if so, what form might that collaboration take?

Poster 2026



Who We Are

Chemistry, Manufacturing, and Control (CMC) statisticians based in Europe, working within pharmaceutical companies and CROs involved in R&D.

We are committed to collaboration and knowledge exchange on precompetitive topics in our field.

2026 Activities: Conferences and Webinars



Nonclinical Statistics Conference (NCS):

Serving on the organizing committee for this year's conference.
Padua, September 23 - 25



Past Webinar:

AI and Statisticians - On Route to Strategic Partnership
Tuesday, March 24th, 2026

CMC Statistical Network Europe

Our Mission

Applying statistics, data science, modeling, and computational methods to advance CMC technical development.

- Serve as a platform for CMC statisticians in Europe to provide input on regulatory guidelines
- Organize workshops to share technical insights, novel methodologies, and established approaches.

2026 Activities: Input on Regulatory Guidelines



Expected f2 Position Paper Submission:

Authored a position paper outlining fundamental statistical flaws and rejection recommendations for the 'expected f2' method.



ICH Q6 (Specification Setting) Position Paper:

Authoring an industry position paper to align manufacturing capabilities with patient risk.

Our Focus

- Support the enhancement of policies and regulations governing statistical practices and guidelines specific to the CMC domain.
- Elevate statistical practices in design, computing, evaluation, and reporting within the CMC field.
- Foster research to create tools that enhance decision-making and deepen the understanding of scientific studies in the CMC space.

Steering Committee

Name	Company
Kevin Lief (Chair)	GSK
Jens Lamerz	Roche
Martin Otava	Johnson & Johnson
Beate Presser	Boehringer-Ingelheim
Christian Schmid	Roche





Webinars



Time for Statistical (r)Evolution

- Stephen Karehu Karanja: Leveraging DoE in dissolution development and robustness evaluation
- Thomas Hoffelder: Equivalence of Dissolution Profiles
- 71 participants



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Stability Modelling: New Tools and Approaches



- Warren Roche (Sanofi): A universal tool for stability predictions of biotherapeutics, vaccines and in vitro diagnostic products
- Bernard Francq (GSK): Accelerated stability studies: a hybrid frequentist-Bayesian approach
- Thomas Zahel (Körber-Pharma): Advanced Hybrid Kinetic Modelling Using Physics-Informed AI for Stability Data
- [Link](#)
- 55 participants



AI and Statisticians



- Tina Lang (Bayer): The Importance of Being Human
- Christian Schmid (Roche): Statistical Frameworks for Computerized Validation of Generative AI
- [Link](#)
- 96 participants

Round table discussion

Round table discussions

- **Panel discussion on Stability Modelling**
 - July 2025 Round table discussion on stability modelling and ICHQ1/Q5C
 - Pierre Lebrun - Cencora
- **Panel discussion on ICH Q6b Specifications**
 - Dec 2025 Round table discussion on specification and ICHQ6
 - Panel discussion on ICH Q6b Specifications | PSI on Glue Up
 - Thomas Zahel - Körber

Position Paper on 'Expected f2' method in Dissolution Testing



Expected f_2 WG



- Listen & learn focus group meeting of the EMA Quality Innovation Group
- Concern on flawed methodology in EMA and South Korean MFDS
- White paper completed and published at ArXiv
- Presented to IQ Disso WG
- Publication in peer-reviewed journal planned
- Participants: Boehringer, J&J, Organon, Roche, GSK, Novo Nordisk; Observer: SwissMedic



Expected f_2 WG

- <https://arxiv.org/abs/2607.16759>



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arXiv

Statistics > Methodology

[Submitted on 18 Jul 2026]

EFSPi CMCSNE SIG position on the 'Expected f_2 '

Thomas Hoffelder, Marijn Clement, Stephen Karanja, Marta Regis, Marc Lindenberg, Filip Vestin, Eleonore Pablik, Marion Berger, Valgeir Einarsson, Helen Thomas, Kevin Lief, Jens Lamerz

The method called 'expected f_2 ' ($\hat{f}_{2,exp}$), as proposed by Noce et al. (2020) and Xu et al. (2021), has been adopted in two health authority guidelines for dissolution profile comparison when variability precludes the use of the conventional similarity factor $\hat{f}_2$. This position paper, developed by a working group of the European Federation of Statisticians in the Pharmaceutical Industry CMC Statistical Network Europe Special Interest Group (EFSPi CMCSNE SIG), presents a critical evaluation of this method. Fundamental concerns are identified. First, the formula for $\hat{f}_{2,exp}$ has no traceable origin in the references cited by its proponents. Noce et al. (2020) and Xu et al. (2021) attribute $\hat{f}_{2,exp}$ to Shah et al. (1998) and Ma et al. (1999, 2000), but neither mentions nor suggests it. Second, no mathematical justification has been provided for the formula. Where Shah et al. (1998) subtract a variance term to reduce the upward bias of $\hat{f}_2$, the $\hat{f}_{2,exp}$ formula adds this term, thereby increasing rather than correcting the bias. This has also been noted by FDA statisticians Liu et al. (2024). Third, the method exhibits poor statistical properties: for highly variable profiles, the variance term dominates the statistic, resulting in low power even as the true difference between profiles approaches zero. The method can reject equivalence when profiles are identical. Fourth, the formula as published by Noce et al. (2020) contains a notation ambiguity that renders the intended grouping of terms unclear. This ambiguity has propagated into regulatory guidance.

A survey of working group members, designed to elicit arguments both for and against the method, found no scientifically meaningful advantage.

The EFSPi CMCSNE SIG concludes that $\hat{f}_{2,exp}$ should not be recommended for dissolution profile comparison.

Comments: 16 pages, 1 figure. Position paper of a working group of the European Federation of Statisticians in the Pharmaceutical Industry (EFSPi), CMC Statistical Network Europe Special Interest Group (CMCSNE SIG)

Subjects: **Methodology** (stat.ME); Applications (stat.AP)

MSC classes: 62P10, 62F03

Cite as: [arXiv:2607.16759](https://arxiv.org/abs/2607.16759) [stat.ME]

(or [arXiv:2607.16759v1](https://arxiv.org/abs/2607.16759v1) [stat.ME] for this version)

<https://doi.org/10.48550/arXiv.2607.16759> 

Submission history

From: Jens Lamerz [[view email](#)]

[v1] Sat, 18 Jul 2026 10:52:08 UTC (780 KB)



ICHQ6 WG



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- Participants: Roche, J&J, GSK, Körber, Ascendis Pharma, Boehringer
- First draft under construction: White paper in construction and will be published at ArXiv
- Present structure/ content of the paper
 - Manufacturability: sources of variability, variability vs uncertainty, method variability, stability
 - Clinical experienced ranges: using of aging effects and clinical proxies
 - Clinical acceptable ranges: understanding CMC influence by PK modelling, clinical designs and further options

Outlook for 2026 - 2027



Outlook for 2026-2027

- Continue with webinars (≥ 1 in 2026, 2-3 in 2027)
- November 2026: NCS short talks
- Pushing forward the white papers and seek to establish more WGs
- Generally striving for more interaction with regulatory agencies



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Please reach out to us

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