International Alliance for Biological Standardization

10th Annual Statistics Workshop:
Science & Statistics – Elevating CMC through Partnership

November 12-14, 2024
IBBR, Rockville, USA

Statistical Science & Statistical Engineering

The engineer-scientist Theodore von Kármán said, "Scientists discover the world that exists; Engineers create the world that never was." Over the centuries, this balancing act of discovery and creation has become one of the main sources of knowledge generation, and economic progress. Statistics is a science, that, as Sir David Cox argues, "provides a unifying set of general ideas and specific methods relevant whenever appreciable natural variation is present." Because natural variation is almost always present in any scientific and engineering study, and because variation introduces uncertainty, statistics becomes the catalyst that allows us to do better science and engineering. This is because statisticians bring a unique skillset as they are trained to think skeptically, to interrogate assumptions, to consider multiple sources of both variation and bias, and to quantify uncertainty.

In this session we will discuss statistical science, statistical engineering, the role of statistics within the scientific method, some key statisticians who were also scientists and engineers, as well as the key role statisticians play as a part of a scientific and engineering team, not in a service-oriented role, but as scientific collaborators that can help solve complex problems.

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Statistical assessment for analytical comparability between pre-change and post-change processes.

On behalf of Aili Cheng and the NCB comparability workstream:

The FDA draft guidance on "Manufacturing Changes and Comparability for Human Cellular and Gene Therapy Products" (2023) recommends statistical approaches such as quality ranges and equivalence tests to assess manufacturing analytical comparability between pre-change and post-change processes. The Critical Quality Attribute (CQA) data underlying such analyses in the fields of cell and gene therapies are highly variable and usually have a limited number of batches. Thus, it is a challenge to demonstrate comparability with enough statistical power. Furthermore, the CQAs may not always follow a normal distribution and the standard approaches which assume normality may not be optimal for these data. Naively applying quality ranges and equivalence acceptance criteria (EAC) solely based on some multiplier of standard deviation (SD) could lead to misleading results, with safe and effective products being discarded. This presentation will focus on key topics relating to comparability in cell and gene therapy, such as study design, acceptance criteria, sample size and important assumptions about the distributions of the data. Additionally, insights from correlational analyses between CQAs and clinical outcomes can be leveraged to assess whether or not the observed ranges and/or results of comparability studies may be meaningful from a practical, scientific and clinical perspective.

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Session I: Science & Statistics

Although often overlooked, statisticians play a key role in the practice of science. Generation of high-quality evidence requires study designs and analyses that align with the scientific questions of interest. Furthermore, coordinated development of study designs and analyses can result in more efficient studies that optimally address important sources of variation. Statisticians bring a unique skillset to this process, as they are trained to think skeptically, to interrogate assumptions, and to consider multiple sources of both variation and bias. Yet statisticians are often only involved at the end of this process, as Sir Ronald Fisher captured in his 1938 Presidential Address to the First Indian Statistical Congress, : "To consult the statistician after an experiment is finished is often merely to ask him to conduct a postmortem examination. He can perhaps say what the experiment died of." Forty years later, Prof. George Box in his Presidential Address to the 138th meeting of the American Statistical Association commented: "By invention of the concept of Experimental Design, Fisher promoted the statistician from a curator of dusty relics to a valued member of a scientific team, responsible for planning and taking part in the conduct of an investigation." Eighty years later, then ASA President Lisa LaVange echoed Fisher's sentiment in her 2018 presidential address when she decried the misuse of statistics in pharmaceutical science, saying "Statisticians to the rescue, please!".

This session will discuss some key statisticians who were also scientists, as well as the key role statisticians play as a part of a scientific team. The session will also include the perspective of scientists and engineers on how they partner with statisticians, as a catalyst for better science and engineering. We will discuss how to promote statisticians as scientific collaborators.