ABOUT

ENLIGHTEN SCIENTIFIC is a technical consultancy founded by me — John F. Miller — in early 2017. After 24-years of working in the pharmaceutical industry I decided to retire from the only company I had worked for — GlaxoSmithKline. I began my GSK career in 1993 working on the Phase III formulation and device development of metered-dose inhalers (MDIs). This is one of the most — if not the most — complex delivery platforms. In the early 2000's I became the CMC leader for one of GSK's new block-buster MDI products for the North American market — ADVAIR® HFA Inhalation Aerosol — and a key technical contributor to the life cycle management of its Rest of World equivalent — Seretide® MDI. I steered the product through NDA submission and, through my various areas of expertise, the product was approved in mid-2006.

Following launch, I remained within Product Development but became increasingly involved in life-cycle maintenance of not only ADVAIR but other MDI products manufactured globally. Although I found the late Phase III and early post-launch activities stimulating and challenging, the last few years became more repetitive with fewer opportunities to fully apply my skills. A series of organizational changes in the mid-2010's led to my transfer out of R&D and into the manufacturing company. I began to question whether I would remain with the company or seek an alternative path that would allow me to apply my expertise in the most productive and valuable ways possible. The uncertainty of my future led me to review my career with GSK. I noticed common features of the activities that gave me the most satisfaction and provided most value to the company, and those that least interested me.

By 2016, it was clear to me that the opportunities simply did not exist within the manufacturing organization to deploy me in the most productive manner for the company or me. During my time with GSK, I learned a tremendous amount about product development and manufacturing, and my own differentiating skills. It was at this time when I decided to leave GSK and establish my own company so that I could find more varied and interesting challenges to exercise my skills and expertise.

COLLOID CHEMISTRY

I gained my PhD in colloid chemistry in 1990 by inventing a method to determine very small electrophoretic mobilities of dispersions in non-polar media. I named the method Phase Analysis Light Scattering (PALS). Today, PALS is the de facto method to measure zeta potential of a wide variety of colloids in many industries. It has been commercialized by a half-dozen leading instrumentation companies. My doctoral studies were under the supervision of Brian Vincent – one of the world's foremost colloid scientists. His research group is considered to have been a world-class center of excellence. I didn't know this when I first started. The following table highlights my areas of expertise. It is not exhaustive but is intended to emphasize the key areas of the science that I can offer greatest value as a technical consultant.

Liquid suspensions	Formulation
Stability	Characterization
Surfactants	Particle size
Zeta potential	Aggregation

In senior high school in the early 1980s my chemistry teacher demonstrated a phenomenon that fascinated me. At the time, I had no idea that it would be the focus of my doctoral research. A voltage was applied to an opaque orange liquid in a glass U-tube. After a few minutes the liquid became clear at one end. I had just observed electrophoresis of particles dispersed in a liquid – a colloid. My project was partially funded by Glaxo Group Research (now GlaxoSmithKline R&D). Glaxo's interest was to understand the role of surface charge in suspensions of micronized drugs in chlorofluorocarbons and hydrofluoroalkanes (HFAs) used metered-dose inhalers (MDIs). Some people claim the particles to be too large to be considered colloidal but, nevertheless, the classical concepts of colloid stability can be applied. After my PhD studies and some post-doctoral research, I began working for Glaxo in 1993 in the Respiratory Product Development department. Except for a short hiatus in the early 2010s, my career focused on HFA-based MDIs. However, during my time with the company I was able to leverage my colloid chemistry expertise for a variety of dosage forms.

EXPERIMENTAL DESIGN

I have learned during my career that many experimental investigations were inefficient. These were accompanied by a poor understanding by the technical teams of the power of statistical analysis and a similar level of understanding by the statistical teams of the underlying physical basis of the experimental factors being studied. I have a strong skill in designing experiments using statistical DOE techniques that take into account the realistic interactions that will occur on a physical basis and then translate those into a robust and frugal design. For example, I successfully reduced a response surface study for an analytical method that would have required more than 500 manual assays (equivalent to more than 4 FTE weeks) to less than 50 assays.

DOE	Statistics
JMP	Excel (complex macros)
Large datasets	Datamining
Visualization	Pattern finding

Important to designing, implementing and analyzing efficient and robust experiments are the experience and expertise of appropriate software tools. My two primary tools are Microsoft Excel and SAS Institute's JMP. I have written simple and complex Excel macros to achieve goals such as automating retrieving and analyzing data, as well as directly controlling hardware. Where more powerful analysis is required I use JMP. I also use it to create highly visual reports and presentations. For large, confounded and/or sparse datasets I have an innate ability to quickly find patterns that are not readily seen by others. I was the first person to use JMP within product development at GSK and it has become a tool used by the majority of scientists. I apply my experimental design skills across all of my areas of focus described elsewhere.

INSTRUMENTATION

I have significant knowledge and experience of conceiving and developing novel instruments for characterizing a range of subjects. For example, I invented Phase Analysis Light Scattering which has become the de facto method of measuring electrophoretic mobility and zeta potential of colloidal suspensions. This innovation pushed the resolving power of electrophoretic light scattering by three orders of magnitude thereby opening up the ability to determine the zeta potential of particles in hydrocarbons and highly viscous liquids.

Light scattering	Colloids
Image analysis	Aerosols
Wide application	Time saving
Bespoke software	Unmet needs

Other instruments include a streaming potential apparatus for probing the surface electrostatic properties of micronized powders in a pressurized hydrofluorocarbon liquid, an inexpensive instrument to quantify powder flow and study how mixing of two or more powders evolves with time, an inexpensive instrument to measure the direction of a spray emitted from a nozzle, and a timing device to analyze and optimize the manual shaking process for collecting doses from metered-dose inhalers. Most of these examples share common features: inexpensive compared to existing methods, address unmet needs, require bespoke software, and conceived by me independently. I am highly skilled in writing high performance software applications often incorporating low level hardware communication and novel algorithms that can give more information than can be achieved traditionally. I have a strong track record of gaining significant insight into complex issues whether they relate to products, processes or analysis of supply chain variability.

PRODUCT DEVELOPMENT

I have more than 24 years' experience working in the pharmaceutical industry. Most of that time was concerned with liquid suspensions of micronized drug substances for delivery to the lung. Though this work included developing aqueous suspensions for nebulization and pressurized liquid carbon dioxide formulations, by far the most experience and expertise is with the metered-dose inhaler dosage form. I was the CMC leader for ADVAIR® HFA MDI Inhalation Aerosol — a major product for GlaxoSmithKline approved and launch in the US in 2006. I was responsible for developing robust components from many suppliers. Weaknesses in the control of the components led to delays to the Phase IIIb development program and I used my experimental investigation skills to lead the efforts to efficiently identify and resolve the issues. At the same time I used those skills to provide key technical insight to resolving issues with another MDI product that had been recently withdrawn from the European market.

Inhaled products	CMC leader
Manufacturing	GMP
Process development	Method development
Life-cycle management	Regulatory documentation

An important aspect of my work — particularly in resolving root cause analyses — is my ability to design bespoke instruments to quantify properties of the products otherwise unavailable to other traditional off-the-shelf techniques. I led the development of some of these from proof-of-concept to fully validated GMP methods.

The last 5 years of my career with GSK saw my transition from product development to product manufacturing, supply, and life-cycle management. I learned the important difference between the scopes of the two functions including striking an appropriate balance between the need to understand product supply challenges from a data-driven scientific perspective and the pragmatism required to meet the aggressive timescales inherently involved in supplying the market. Through both my late phase development and commercial supply work I have amassed a lot of knowledge regarding efficient use of experimental design, statistics, and analyzing large and/or sparse datasets. These are aligned with industry standard practices such as Quality by Design and ICH guidelines.

Services available

Detailed characterization

Routine measurement

Workshops and Seminars

Consultation

john@enlightenscientific.com
http://www.enlightenscientific.com
(presentation available online)