Exclusive Digest – Workshop Leader Interview with Dr. Dirk Kreder, Founder & CEO, **anteris medical GmbH**

Combination Products Lifecycle Management Summit 2018

In the lead-up to our Combination Products Lifecycle Management Summit (June 19 – 21, Boston), we have caught up with **Dr. Dirk Kreder**, Founder & CEO at **anteris medical GmbH** for his exclusive insights in how the industry is evolving, and what lifecycle management means in the combination products space.

Dirk is a seasoned expert in biotechnology industry. Prior to founding anteris, he spent 8 years on leading teams for development of complex generics and biosimilars. Thereafter his focus shifted to auto-injectors and combination products. Dirk is committed in helping drug and device developers to optimize time-to-market and smooth regulatory approval process in a global environment.

***HW**: Over the last 12 months, "combination product" has become a real buzz word in the industry. There're however still a lot of challenges, from technical to regulatory to commercial, but where do you see the biggest opportunity and what's the major barrier?*

DK: Indeed, the past months have been something like an awakening of industry to the many opportunities and challenges, even though the regulation of combination products is not exactly new. Initially, it seems, many of our colleagues have hoped that most combination product challenges can be contained and dealt with under the label "primary packaging" and it took FDA and EMA to put their foot down forcefully for the new reality to sink in with everyone.

> *What is happening around combination products today is delivering real value to patients, offering newer and less intrusive application of very effective treatment – which will also lend to longer and more valuable life for such products.*

From our perspective, however, overcoming the initial inertia is well worth it. What is happening around combination products today is delivering real value to patients, offering newer and less intrusive application of very effective treatment; giving such products a longer and more valuable life, and even allowing biosimilars a higher degree of differentiation.

The major barrier we see is still dealing with the regulatory consequences on the backdrop of these new opportunities, which are rapidly changing expectations from the market, physicians, patients, and regulators.

HW: *Lifecycle management is obviously a complex subject and involves multiple teams internally. What's the common pitfall? And what's your best tip?*

DK: We actually witness two different sets of challenges almost every day. For many **smaller organizations**, in particular new entrants in the injectable or inhalable market, the focus is understandably on the preclinical and clinical challenges of developing the actual drug. Making it through this phase quickly and successfully is a matter of economic survival. Equally understandably there is often little focus on neither, the opportunities nor the challenges of developing the medical device constituents of the combination product. So, a common pitfall is too little and belated attention to the medical device aspects, despite clear comments and responses from the regulators to almost every dossier we see. The expectation has (almost) always been, still is, and will be for the foreseeable future, that for a combination product, proper design planning is required, acceptance criteria are documented, verified, and validated, the labeling follows drug and medical device regulations, and that risk management is performed and documented following the medical device regulations.

A common pitfall (for SME) is too little and belated attention to the medical device aspects, For larger organizations, the challenge of embracing unfamiliar regulations is a common theme.

For **larger organizations** with ample resources it is more often the "have always done it this way" syndrome that can get in the way. We also see the challenge of (such organizations) embracing new or unfamiliar regulations, from a field our colleagues in biopharma are not automatically familiar with. Having worked for some of those, I can assure you that there is a long list of examples.

In either case, it might be useful to enlist outside support, even if it is just for a gap analysis, or implementation of processes which would otherwise get delayed or hindered by internal challenges and concerns.

HW: *Given you've worked with both US and European markets, what's the major difference when it comes to combination products?*

DK: Really, surprisingly little difference. From our daily work we find that regulators in the US and Europe are actually quite closely aligned on the most important principles and processes even if they use different terminologies and solutions to the regulatory challenges at hand. We find that the spirit and approach regulated under 21 CFR part 4 works very well in both markets, with a few tactical differences in how to achieve clearance. We frequently go back to the famous two-sided table FDA published in their guidance to determine the missing parts in customers development programs, whether the combination product starts as a drug product, or a medical device.

HW: *Traditionally lifecycle management refers to legacy products. With the increase in biosimilars and generics, and connected device platforms, it seems combo products developers need to start thinking about LCM at launch, or even before. What's your thought?*

Burdensome as it may seem, 21CFR Part 4 has given the biopharma originators a new and attractive LCM instrument as the regulation applies to everyone.

DK: You are absolutely right that the strategies and tactics of LCM are changing. The two most prominent avenues during my pharma days were new clinical indications or patient populations, or the combination products of the last century primarily refer to combining two different APIs into one drug product. Both strategies fail as effective protection against generic competition. New clinical indications are often included into generic/biosimilar approvals by extrapolation, and API sourcing is a matter of opening a catalogue. There is another important flaw with these two LCM strategies: they typically cost the originator much more time and money than the generic competition.

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Burdensome as it may seem for biopharma companies, 21 CFR part 4 has given the originator a new and attractive LCM instrument as the regulation applies to everyone. For example, developing a new on-body patch pump and clearing it as a combination product just before or even after patent expiry is super-disruptive for the biosimilar competition, and therefore you see a burst of activities at companies like Amgen, Roche, and more or less everywhere else in pharma.

To answer your question with a short statement: yes, LCM strategies for both, originator and biosimilar companies are extremely important and cannot be defined too early.

***HW**: Can you give us a snapshot of your workshop session, and what can attendees anticipate?*

DK: The workshop will open with a concise summary of the current regulatory and market situation, tailored to the participants' background and interests.

The focus will then shift to tactical and strategic lifecycle management of combination products, with plenty of examples from both the US and the EU markets.

As many LCM approaches tap into platforms offered by solution providers, we will also discuss our experience and lessons learned from working with platforms, and review how this changes the requirements for the drug company.

The workshop is aimed to be interactive, and we expect and encourage participants' contribution to enable joint learning in a closed-door setting.

Dr. Dirk Kreder will be leading an interactive preconference workshop at this summit on **Tuesday, June 19**, on:

Lifecycle Management of Combination Products (08:00 – 11:00)

Combination products, as the term implies, draw from the pharmaceutical and the medical device industries, and force developers and regulators into a complex and challenging evaluation of opportunities and risks. From a commercial perspective, market players act to prolong the commercial life of a product, counter a competitor's move, increase the products value by offering additional value to the patient, or simply bring a product up to the standard of care. Whatever the change to the product, a series of regulatory, commercial, or supply chain consequences have to be considered to make the effort successful.

The workshop is intended to develop a comprehensive and actionable framework for decision makers or development teams in an interactive fashion, allowing participants to

- Gain **an overview of market trends and ongoing changes** in the combination product market
- Assess the **expected regulatory consequences of LCM changes** to a combination product
- Evaluate **commercial strategies** regarding their likelihood of achieving the **intended goal and their competitive value**