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Rise of Complex Injectable and Drug Device Combination

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Invited Editorial

Rise of Complex Injectable and Drug Device Combination

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The pharmaceutical industry has experienced sensational revolution over the last six decades. The first generation novel drug delivery systems (e.g., oral sustained release preparations, inhalations, transdermal patches, etc.) were developed rapidly during three decades (1950–1980), achieving high product translational competence. Spansule® technology comprehended a sustained release of the drug over a period of 12 hours for the first time in 1952. After four years of that incidence, pressurized Metered Dose Inhalers (MDI) initiated the history of inhalation delivery systems. With the approval of Scop® in 1979, the transdermal patch was made available in the market. In the second generation pharmaceutical formulations, the central issue was focused on nanomedicines and smart delivery systems. Although the second generation novel drug delivery systems (e.g., liposomes, nanoparticles, microspheres, gene delivery systems, etc.) engrossed lot of focus during 1980-2010, there are very limited products available in the market currently. Doxil® (liposomal formulation) evolved as the first nanomedicine in 1995. The first nanotechnology-based target drug delivery system (Abraxane®) was made commercially available in the market in 2005. The marketable and commercial success of these nano-drug delivery systems/platforms attracted a large number of followers. Presently, there are about 6,400 platform technologies available worldwide, out of which 4,800 are active and 41% of these technologies are injectable dosage forms. Hence it can be stated that "The new era is all about Complex Injectable formulations".

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Complex injectable are the medicines that generally have at least one feature that makes them difficult to "genericize" under traditional generic approval approaches. Complex Injectable market is gaining traction in injectable therapies owing to the increase in their use in life threatening as well as chronic disease therapies.

The complexity may be with respect to the Active Pharmaceutical Ingredient (API) or the product manufacturing process or route of administration, or it could even be the delivery device involved. Due to the higher degree of complexity involved, the competition for manufacturing such products is relatively less as it requires major capital investment for establishment of desired facility. Every individual product may have unique manufacturing process requiring specific set of equipment for batch manufacturing. Therefore, growth in the complex injectable market is largely driven by their complex generic formulations. Market for complex injectable is primarily driven to meet the unmet need of patients or to encounter increasing rate of chronic diseases, minimizing toxic effects of drugs through advance technology platforms, increase in the demand of self- administration devices for patient convenience, better product stability or targeted delivery of drug products.

Complex Injectable (generics) are exceedingly challenging and it is quite difficult to prove similarity through pharmaceutical equivalence or bioequivalence studies. The Food and Drug Administration (FDA) is keen to learn about the differences between the Reference listed drug product and the generic drug product, rather than their similarity. So there is a requirement of immense characterization of these products through orthogonal techniques. Apart from the popular

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liposome and microsphere formulations, the other platform technologies that are currently available commercially are: Lipid based products, PEGylated products, Polymer drug and protein drug conjugates, Nanoparticle/Nanocrystals, Micelles, Cyclodextrin complexes, Emulsions, Suspensions, Super Critical Fluid technology, Linker based technology, just to name a few. A simple way to start the development of Complex Injectable is to first assess regulatory requirements followed by preparing a clear road-map and development strategy. An early engagement with FDA would be beneficial before starting any investment on the manufacturing facility or initiation of extensive characterization work or biostudy/ clinical trials etc. Product specific guidance issued by the regulatory agencies are of much help to remain in right track of development.

The self- administration devices are also called "Combination products" which may be a combination of Drug/Device or Biologics/Device or Drug/ Biologics or Drug/Device/Biologics regulated and sold as a single unit. They are usually prefilled syringes or cartridges that are inserted into auto-injectors or pen devices. The devices could be re-usable or disposable type and may be designed to deliver single or variable doses. These combination products are off-late guided by several stringent regulatory requirements to ensure safety, dosage accuracy, patient convenience or any other critical functional tests designated for its intended use and performance since they are to be used by the patient himself or herself majorly. Creating strategies for device development as well as its clinical requirement at very early stage of product development like Human Factor study needs would de-risk the huge investment and also fulfill all the regulatory requirements of maintaining a systematic Design History File.

The next generation injectable that would make a steady access in the pharmaceutical industry are micro devices which range from simple tongue depressors to micro-chip based implants, smart injector pen platforms to monitor dosage delivery as well as timings, wearable devices for infusions, etc. In the future, the discovery of new molecular entities may be combined simultaneously with advanced delivery technologies to make the drug candidates into more ideal and therapeutically effective formulations.

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