FORMULATIONS AND PROCESS INNOVATIONS: QBD APPROACH AND PAT TOOLS SUPPORTED BY ARTIFICIAL INTELLIGENCE TECHNIQUES

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QbD (*Quality by Design*) and PAT (*Process Analytical Technologies*) concepts significantly facilitate the implementation of new technologies in the pharmaceuticals´ formulation and processes development. From simple formulations to complex delivery systems, QbD approach allows identification of the critical process parameters and material properties affecting the pharmaceutical products quality. For the analysis of complex relationships, establishment of the design space and, most importantly, control strategies, modeling and simulation tools are of paramount importance (1). Hybrid models, which combine elements of mechanistic modeling and empirical approach, are particularly important for processing of large amount of data collected by monitoring the process with PAT tools. This enables the establishment of a virtual copy (digital twin), or cyber-physical system, which facilitates the optimization and continuous improvement of the process. Artificial intelligence techniques in formulation and process innovations involve different machine learning algorithms. They are used to solve regression or classification problems and to process data of various types (numerical, textual, images, etc). Artificial neural networks can be applied from the initial formulation development to the production of validation batches for which the bioequivalence predicted by models has been confirmed (2). Artificial intelligence technology is also very important for the design and application of virtual copies of continuous production processes or complex biotechnological processes. This facilitates the implementation of the Real Time Release Testing (RTRT) strategy. It is to be expected that good modeling practices will be more precisely defined through the official regulatory guidelines, in the context of the application of artificial intelligence techniques.

References

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INOVACIJE U FORMULACIJI I PROCESU: QBD PRISTUP I PAT ALATI PODRŽANI TEHNIKAMA VEŠTAČKE INTELIGENCIJE

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QbD (*Quality by Design*) i PAT (*Process Analytical Technologies*) koncepti značajno olakšavaju implementaciju novih tehnologija u razvoju formulacija i procesa za proizvodnju farmaceutskih preparata. Od jednostavnih formulacija do kompleksnih nosača, QbD pristup omogućava identifikaciju kritičnih procesnih parametara i karakteristika materijala koji utiču na kvalitet farmaceutskih proizvoda. Za analizu kompleksnih veza, uspostavljanje *design space*-a i, što je najznačajnije, kontrolne strategije od izuzetnog značaja su alati za modelovanje i simulacije (1). Hibridni modeli, koji kombinuju elemente mehanističkog modelovanja i empirijskog pristupa su naročito značajni za obradu velikog obima podataka koji se prikupljanju praćenjem procesa PAT alatima. Na taj način se omogućava uspostavljanje virtuelne kopije (*digital twin*), odnosno sajber-fizičkog sistema, čime je olakšana optimizacija i kontinuirano unapređenje procesa. Tehnike veštačke inteligencije koje se primenjuju u kontekstu implementacije QbD i PAT alata u formulacionim i procesnim inovacijama podrazumevaju različite algoritme mašinskog učenja. Koriste se za rešavanje regresionih ili klasifikacionih problema i obradu podataka različitog tipa (numerički, teksutalni, zapisi u slikovnom formatu, itd). Veštačke neuronske mreže mogu da se primene od inicijalnog razvoja formulacije do proizvodnje validacionih serija za koje je potvrđena bioekvivalentnost predviđena modelima (2). Tehničke veštačke inteligencije su takođe veoma značajne za dizajn i primenu virtuelnih kopija procesa kontinuirane proizvodnje ili kompleksnih biotehnoloških procesa. Na taj način se olakšava implementacija strategije puštanja leka u realnom vremenu (*Real Time Release Testing*, RTRT). Za očekivati je da se i kroz smernice regulatornih tela preciznije definišu dobre prakse u modelovanju, u kontekstu primene tehnika veštačke inteligencije u podršci QbD i PAT koncepata.

Literatura
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