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Recent developments regarding a Novel Excipient Qualification process

The International Consortium for Innovation and Quality in Pharmaceutical Development (IQ) and the International Pharmaceutical Excipients Council of the Americas (IPEC-Americas) are working toward accelerating excipient innovation and ways to bring forth novel excipients with enhanced functionality that improve drug delivery and manufacturability (e.g., continuous manufacture) and that focus more on the needs of special populations (e.g., pediatrics). This collaboration led to a Critical Path Initiative Meeting (CPIM) with the FDA on March 10 to discuss developing an independent Novel Excipient Qualification process that encourages the development of innovative novel excipients and their use.

The current process for drug product approval doesn't include a mechanism to independently evaluate novel excipients. Rather, they are evaluated as part of a drug product. Pharmaceutical companies thus face uncertainty in using novel excipients because of regulatory authority acceptability concerns with an excipient not listed in the FDA's Inactive Ingredient Database (IID). Without some assurance that regulators will find a novel excipient acceptable—based on an approved process and on appropriate safety information provided in a drug application—pharmaceutical companies may be deterred from incorporating novel excipients into their drug products, thereby limiting benefits to patients.

The need for novel excipients has never been greater, nor the benefits clearer. In the best case, the absence of suitable excipients is slowing development, resulting in less than optimal performance and delaying products from reaching patients. In some cases, the development of promising therapeutic entities is being discontinued, leading to negative implications for

patients. Novel excipients with improved properties can enable better product profiles by improving efficacy, reducing side effects, and increasing ease of use and patient adherence to new therapeutic modalities.

Various types of excipients are currently considered "novel excipients." Here are examples of excipient types that IQ and IPEC-Americas believe should be covered in any future Novel Excipient Qualification process:

- New chemical entities
- Modified excipients (generally polymers of the same family with varying chain length/molecular weight/substitution)
- New co-processed excipients made from two or more previously approved excipients
- Previously used excipients that are employed in a new route of administration or patient population
- Excipients used in an approved drug product but at a higher level of use than previously listed in the IID
- Approved food-use/cosmetic-use ingredient.

Establishing a qualification process for innovative novel excipients could alleviate uncertainty associated with developing new therapeutics with improved product profiles. Although novel excipient review processes have been proposed, they haven't yet provided sufficient assurance of the acceptability of such materials outside the drug application system. An independent qualification process would stimulate innovation within the excipient industry and encourage pharmaceutical companies to evaluate novel excipients for the benefit of patients.

IQ and IPEC-Americas conveyed to the FDA that, currently, there are limited incentives for pharmaceutical companies to use novel excipients (not listed in the IID) in new formulations due to the uncertainty of their acceptance in new drug product applications.

IQ and IPEC-Americas proposed an independent Novel Excipient Qualification process (outside of the drug approval process) to the FDA as a possible approach to novel excipient regulatory acceptance. The program would be based on supportive studies and include a publicly available "qualified novel excipient list" for manufacturers to reference during drug development.

The CPIM was attended by about 40 FDA staff from various offices and divisions and was a great success.

The CDER Office of Product Quality (OPQ) recognized the need for novel excipients as a gap in manufacturing innovation. OPQ supported the concept of novel excipient availability and use independent of specific drug products. OPQ is interested in discussing both the concept and its advancement further. The FDA is currently working with IQ and IPEC-Americas to schedule another meeting with CDER leadership to discuss collaboration and how a qualification process might work.

These discussions are very encouraging and IQ and IPEC-Americas hope that they lead to a Novel Excipient Qualification process that works for the FDA, industry, and—most importantly—patients.

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