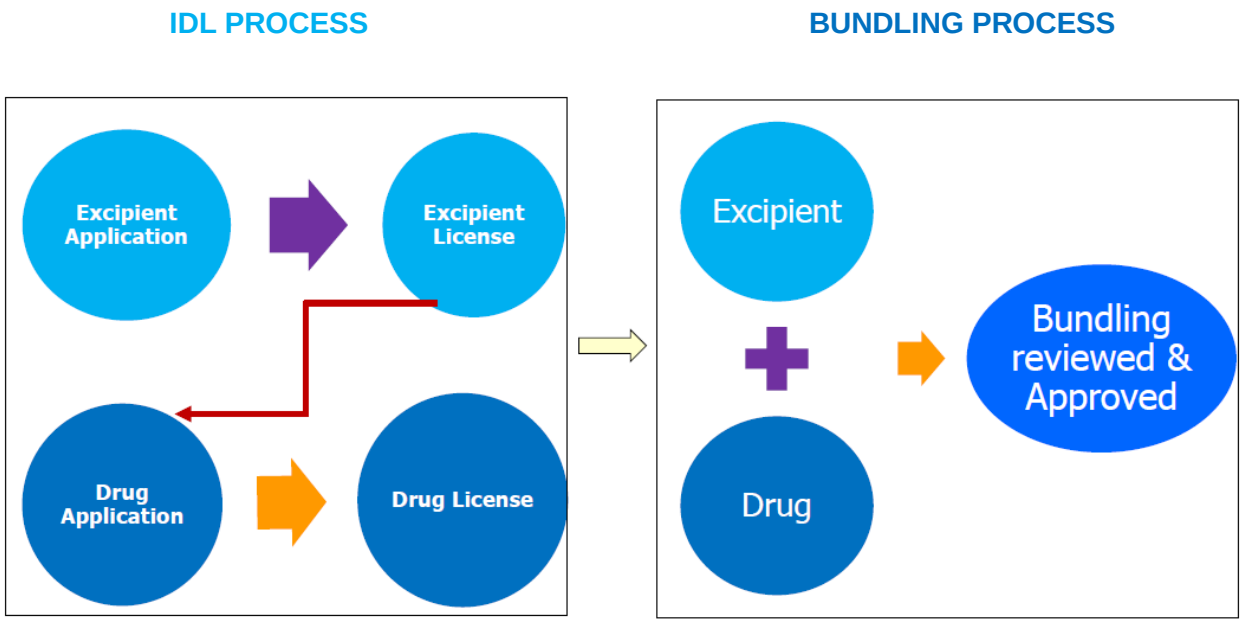
IPEC AMERICAS insider

CFDA Order 134 – Quite a Bundle for Excipient Makers Selling into China

Chinese FDA (CFDA) Order 134 "Matters Concerning Bundling Review and Approval of Pharmaceutical Packaging Materials, Pharmaceutical Excipients and Drugs"[1] took effect on August 10, 2016. This order provides for the approval of pharmaceutical packaging materials and excipients in conjunction ("bundled") with drug product applications. Previously in China, packaging materials and excipients could be reviewed independently via the Import Drug License (IDL, Drug Licensing) process. Although this new system of "bundling" of excipients and packaging materials with the drug product approval brings China into line with the US and Europe, both of which already review excipients only in conjunction with drug applications, there are still many differences in the drug approval processes between the three regions.

In this new approval process, the "Approval Number" (AN) issued by the CFDA for the entire application will act as the confirmation that the excipient is permitted for use. Figure 1 compares the previous process (Drug Licensing) with the new "Bundling" process[2].

Figure 1 – Previous Drug Licensing Process vs. New Bundling Process



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[1] Translations from documents issued in Chinese language are for reference only. The original shall prevail.
[2] Illustration courtesy of Colin Li, Chair, IPEC China

The implementation of the new bundling process as compared to the Import Drug License (IDL) process for excipients is somewhat confusing. Table 1 summarizes the various scenarios that excipient manufacturers may face with their excipients and how the new CFDA order affects them. It is important to note that the final row, "Other pharmaceutical excipients specified by CFDA" allows the agency other options to deal with situations that may not have been addressed or contemplated when this order was issued.

Table 1 – Use of IDL Process vs. Bundling Process for Excipients

"AN" – requires excipient to be bundled with drug product application ("Bundling Process")
"IDL" – bundling not required for excipient ("IDL Process")

	Drug product already marketed in China	**New Drug Product (to be marketed in China in future)**	**Drug product already being imported into China**	**Drug Product to be imported into China in future[3]**
New excipient (never used in any approved drug globally)	Not Applicable	AN	Not Applicable	Waived[5]
Excipient without IDL or Approval Number but used in drugs outside China	Not Applicable	AN	Waived[5]	Waived[5]
Excipient with IDL, no change in route or use level	IDL[4]	AN	Waived[5]	Waived[5]
Excipient with IDL, but change in route of administration or use level	AN	AN	Waived[5]	Waived[5]
"Other pharmaceutical excipients specified by CFDA"	AN	AN	Unknown	Unknown

The CFDA order also references "High-Risk Pharmaceutical Excipients" which include excipients from animal or human sources; excipients used in inhalation, injected, or ophthalmic drugs; excipients supervised under special requirements by the CFDA; and new excipients (those which have not been used in marketed drugs in China or elsewhere, see Table 1 above).

This order is obviously very new and it remains to be seen how it will be implemented in practice. The Chinese FDA expects that there will be a transition period during which more details and implementation guidance will be become available.

Meanwhile, it is advised that excipient manufacturers doing business in China keep a close eye on this important new rule and any consequences and new information that result from it. IPEC China (www.ipec-china.org) is closely monitoring this situation and provides updates as appropriate to its members.

[3] Considered to be "High-Risk Pharmaceutical Excipient"

[4] May continue to be used after the expiration period of registration certificate. All expiration periods extended to 31-Dec-2017.

[5] Follow provisions of SFDA Order No. 28, Article 95 http://eng.sfda.gov.cn/WS03/CL0768/61645.html