



The IPEC Novel Excipient Safety Evaluation Procedure
IPEC-Americas Safety Committee
April 2007

Introduction

The Regulatory Affairs and Safety Committee of the International Pharmaceutical Excipients Council of the Americas (IPEC) have been charged with developing a proposal for a global Novel Excipient Safety Evaluation Procedure. At present, "new" excipients can only be reviewed in the US as a component of a New Drug Application, Abbreviated New Drug Application or Biologics License Application, and the definition of "newness" is unclear. For example, the degree of "newness" for a previously approved excipient proposed for an unapproved use or a minor chemical modification of a previously approved excipient might be different than that for a new chemical entity. The regulatory environment appears to be similar in other parts of the world, but in most countries, guidelines on this subject simply do not exist.

The uncertain regulatory environment is a substantial barrier to development and introduction of new excipients to the marketplace: Pharmaceutical manufacturers are reluctant to include potentially "new" excipients in their drug applications. Potentially more beneficial excipients can be researched or may have been developed but excipient manufacturers have no incentive to further develop and commercialize them. The proposed IPEC Novel Excipient Evaluation Procedure attempts to remedy this situation by instituting an independent evaluation procedure for assessing the safety of new excipients.

Overview

To fill the regulatory gap in the area of new excipient regulation, IPEC has contracted with Aclairo Pharmaceutical Development Group, Inc., (Aclairo) a consulting firm headquartered in Vienna, Virginia to form, administer, and manage a "Novel Excipient Evaluation Committee" ("NEEC") whose primary function will be to evaluate compliance with "Guidance for Industry: Nonclinical Studies for the Safety Evaluation of Pharmaceutical Excipients (<http://www.fda.gov/cder/guidance/5544fnl.htm>)" published by FDA in May 2005. The ICH has no specific excipient safety evaluation guidelines, but the FDA guidance cites ICH safety testing guidance documents as reference materials for the conduct of safety tests.

Excipient manufacturers (sponsors) will submit, to Aclairo and the committee, a dossier in CTD format containing available safety information for a specific excipient on a fee-for-service basis. A committee review panel will then evaluate the information in the context of the FDA and/or appropriate ICH guidance documents, issuing a statement of conformance or nonconformance to the sponsor. The evaluation will be limited to safety and chemical characterization only as it relates to safety.

If the review panel concludes that the requirements of the FDA and/or ICH guidance documents are not met, it will recommend specific steps necessary to bring the application into compliance. The sponsor will then have the opportunity to resubmit the application with the requested changes.

The panel's report will be owned by the sponsor and released at their discretion. For example, the sponsor would have the option of using the panel's conclusions when marketing their product. In addition, the sponsor could include the report in the appropriate Drug Master File or New Drug Application.

Committee Administration

IPEC will identify technical and scientific experts qualified to serve as NEEC panel members. A list of these experts will be provided to Aclairo, and these experts will form the basis for the NEEC roster. Aclairo staff will maintain the NEEC roster which will include information on the expertise and interests of each member. An introductory meeting of all NEEC members will be held to acquaint them-to the process, communicate committee objectives and choose a committee chair. Update meetings will be held periodically as needed. At least one third of the reviewing committee, including the chair, will be rotated every two years to maintain continuity.

A contract will be signed between Aclairo and each member of the roster indicating willingness to participate, appropriate remuneration, and timeframes for review. Panel members will be instructed to disqualify themselves from deliberations over specific products if they or another panel member deems a conflict of interest exists. Panel members not meeting their contractual obligations may be terminated from the roster. In addition, panel members will be required to sign a detailed confidentiality agreement with Aclairo.

Sponsors will be responsible for appropriate application fees, which will cover projected consulting and other committee expenses.

Once an application is received, the Committee Chair will determine the appropriate areas of expertise necessary to review it and will in turn forward the application to three appropriate committee members (the Review Panel). The review panel will review each application according to the objectives determined by the IPEC Safety Committee. Once all three reviewers reach agreement, they will issue their conclusions directly to the sponsor.

Review Panel Guidelines

Aclairo staff will send copies of the application to each panel member at the appropriate time. Panel members will then conduct an initial review of the application and hold an introductory conference call or meeting, at which a chair will be chosen for the specific application. The chair shall prepare agendas for and conduct subsequent meetings as well as organize the panel report.

The panel will meet as many times as is appropriate to review the data submitted for the new excipient and to prepare a report containing its conclusions and recommendations for the safety of the new excipient. Any decisions before the panel shall be decided by a unanimous

vote of the members serving on the panel for the new excipient. Dissenting views and opinions shall be noted in the panel report.

Panel members will be instructed to conduct their review in accordance with IPEC-Americas Safety Committee guidelines. Consideration of similarities with approved and/or tested materials will be encouraged.

Meetings shall be conducted informally and can be via conference call or "face-to-face." Electronic communication is also appropriate between meetings.. All panel meetings shall be closed and no outside contacts are permitted to attend and all correspondence will be treated as confidential.

The panel shall prepare detailed minutes of the meeting and conference calls. Minutes should include a complete and accurate description of the matters discussed and conclusions reached. A transcript of the panel meeting is not required.

If an issue arises during the review of the data, an expert specializing in the area of concern may be consulted after the discussion with the sponsor of the new excipient. However, the panel may not consult with any person who may have data or information for the new excipient without first obtaining agreement from the sponsor of the new excipient.

The panel shall maintain strict confidentiality and the panel will not disclose information discussed at the meeting. A confidentiality agreement will be completed between the panel members, the sponsor, and Aclairo.

Evaluation Conclusions

- The conclusion of the panel's deliberations will be either
 - Meets safety requirements at the proposed concentration for an intended route/form (e.g. oral, topical, ocular, injection, etc.).
 - Does not meet safety requirements for an intended route
- Petitioners will be informed if their product does not conform with the appropriate FDA or international safety requirements and provided with reasons for the conclusion. They will be given an opportunity to remedy the deficiencies and re-submit an amended application.
- Deliberations and conclusions of the review panel are confidential.
 - Petitioners remain in control of the process and may choose to publicize the results and/or incorporate them into the proposed Excipient Master File or a Type VDMF submission at their discretion.