

Beginnings of IPEC and Excipient Harmonization.

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There was recognition nearly ten years ago that duplicative testing of common excipient materials was required by different pharmacopeias, and also by the U.S. *Food Chemicals Codex*. This earlier was identified as a problem at the Interphex meeting in New York City during the open session on "raw materials," April 1987. Both Professor Shangraw and Dr. Grady were on that program.

Food Additives Council At that time it was most concerned with the *Food Chemicals Codex*, a publication of the National Academy of Sciences. There had been harmonization between it and *The National Formulary*, partly because of the flow of leadership from *NF* to *FCC*, i.e., Justin Powers, followed by Durward Dodgen. So that problem was not significant in the United States. The problem did matter for companies buying excipient internationally for use in drug formulations that were made in more than one country.

Jerry Halperin and Tim Grady met with the members of the "Food Additives Council" in DC in 1990 or '91. They advocated that the excipient manufacturers should form an organization in order to present a united view on efforts to improve the standards (NF) for excipients and to relate to the excipients industries in Europe and Japan. Moreover, they even suggested the name, "International Pharmaceutical Excipients Council". The Council was non-responsive. It should be observed here that sales to pharma represented a tiny portion of the large bulks of additives in production, a fact that would turn up repeatedly in any attempt to get that industry to accept standards, notably for Sucrose. The Council thus was not seen as a vehicle for this issue. Something else had to materialize.

The Pivotal Year for Harmonization. As part of its regular Open Conference series, USP had a Spring Conference, Williamsburg, Virginia, May 1989. This was a multi-topic meeting, but one of the topics was a roundtable discussion on excipient standards. Professor Ralph Shangraw had fielded this topic for his Subcommittee on Pharmaceutics 1. At the end of the conference the Subcommittee concluded that harmonization of standards for excipients would be a worthy effort. Almost immediately after, in June 1989, the European Pharmacopoeia was holding a 25th Anniversary Open Conference in Strasbourg, France. Dr. Grady was on the program speaking for USP and was accompanied to that meeting by the new USP Executive Director Designate, Jerome A. Halperin. At that conference USP proposed that pharmacopeias begin harmonization of standards for excipients as a general service to industry worldwide. The idea was resisted within the EP staff and Commission, although well received of course by European industry.

Only a few months later, in September 1989, Japanese industry held a conference in Tokyo, titled the "Future of the Pharmacopoeia." Dr. Grady gave the keynote talk wherein he reiterated the proposal to harmonize standards for excipients, along with a more general treatment of broad range harmonization and the problems, which it could face. During a social gathering amongst the leadership of the Japanese, British, and European Pharmacopoeias, Mr. Halperin proposed the formation of a new organization. The main point project would be harmonization, in addition to general mutual support and education. This became the Pharmacopoeial Discussion Group, which exists yet today. Ph.Eur. subsequently expelled BP at a "quadripartite" meeting in London in the early 1990's.

The first working meeting on actual excipients, Lactose and Magnesium Stearate, was hosted by the USP Excipients Subcommittee in October 1989. Thus, 1989 must be seen as the

pivotal year in the history of pharmacopeial harmonization. The next year, the International Conference on Harmonization of Technical Requirements for Drug Product Registration held its first public international meeting.

IPEC Emerges. The pharmacopeias, again hosted by USP, held the International Conference on Harmonization of Excipients in Orlando Florida, January 1991. In the hotel lobby (not a K-street cabal!), Dr. Grady recalls Professor Shangraw urging Lou Blecher, who was accompanied by Bob Pinco, to form an international excipients manufacturers group, specifically to facilitate work with the pharmacopeias. It seems that Lou also had hopes along that line. All recognized that the Food Additives Council was not going to act on the problem.

There should be no doubt that the close relationship, and mutual respect between Lou Blecher and Professor Shangraw was the fuel that got that organization off its launching pad. It was clear that a new trade organization would not be talking to a brick wall. IPEC was formed and already held a meeting in June, 1991 in King of Prussia, PA.