What to look forward to in GaBI Journal, 2014, Issue 2

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As mentioned previously, non-biological complex drugs (NBCDs) continue to raise important regulatory and practice issues. This issue of the *GaBI Journal* contains a number of manuscripts dealing with these products and begins with an update on NCBDs (nanosimilars) developments by Professor Gerrit Borchard. This is followed by a manuscript discussing the use of size and heterogeneity to characterize liposomal doxorubicin generics (nanosimilars) by Professor S Moein Moghimi and Dr Z Shadi Farhangrazi who raise a number of important issues including how comparisons can be made when innovator products are no longer manufactured or available.

NCBDs are also the topic of a review by Dr J Michael Nicholas. Dr Nicholas reviewed the immunogenicity and exchangeability of NBCDs including liposomal products, glatiramoids, and iron sucrose products and based on his review concluded that 'experience suggests' that NBCDs should receive the same pre-approval scrutiny as follow-on biologicals including preclinical and clinical testing to 'establish similar quality, immunogenicity, safety and efficacy of follow-on NBCDs' and that 'automatic switching or substitution of a follow-on NBCD … should be contingent on demonstration of therapeutic equivalence'.

The naming of follow-on products continues to be an unresolved issue of concern as illustrated by a survey conducted by the Alliance for Safe Biologic Medicines (ASBM). Dr Richard O Dolinar and Mr Michael Reilly present their results of a questionnaire concerning the understanding and use of biosimilar products that was sent to 4,324 prescribers in France, Germany, Italy, Spain and UK who were selected from a global market research panel of likely prescribers of biosimilars. The respondents were offered a modest compensation for their participation. Selection bias is likely since the manuscript presents the opinions of only 470 of the 1,002 prescribers who responded. Also, the ASBM has potential conflicts of interest since it has innovator pharmaceutical members/support. However, the responses clearly indicate some major areas of concern including practitioner misunderstanding of biosimilar products and how they are approved, as well as how practitioners record important product information in medical records. Of particular concern is that the recording practices reported by these practitioners would essentially prohibit adequate post-marketing surveillance of follow-on biosimilar products.

The issues raised by the ASBM 2013 prescribers survey relate to the interchangeability of follow-on products. Dr Hans C Ebbers and Mr Paul Chamberlain in their review of the interchangeabilty of monoclonal antibodies present a somewhat opposing view. These authors suggest that 'it will be highly challenging to establish interchangeability' and 'question whether the 'higher' standard required for designation of interchangeability adds to the benefit of patients'.

Readers, patients, caregivers, pharmaceutical manufacturers, regulators, and third-party payers are all facing difficult decisions concerning the cost/benefit analyses of decisions about how to approve, name, switch or substitute follow-on generic products. *GaBI Journal* is committed to presenting all sides of these difficult but important decisions. Clearly, there is much to be learned about the science, regulation, and clinical use of such products; not only for the complex, difficult or impossible to characterize biologicals and NBCDs but also for simple chemical generics as illustrated by other manuscripts in this issue discussed below.

A manuscript by Kumar et al., for example, also used a questionnaire to examine practitioner opinions of simple chemical generic drug products. The questionnaire was completed by 18 specialist practitioners from a number of private medical centres in Malaysia. These practitioners, while positive towards the use of generics were 'cynical about the quality in terms of efficacy and safety of some drug categories'. These authors suggested that there is a need for educational programmes to educate physicians about the role of Malaysian regulators in approval of generic drug products.

Questions about the adequacy of current generic drug regulatory approval processes however were raised in a systematic overview by Eckstein et al. of the safety parameters, pharmacokinetic properties and regulatory approval of tyrosine kinase inhibitors. They point out that these drugs have narrow therapeutic indices, that toxicity evaluations may take many years to complete, and that the fact that they are taken orally is significantly different from IV cytotoxic oncology drugs. Based on their review these authors suggest that 'product specific guidance is needed to accurately perform bioequivalence studies and … marketing authorization applications' for these important targeted oncology drugs before the expected appearance of the first tyrosine kinase inhibitor generic products.

The use of the generic immunosuppressive drug mycophenolate mofetil is discussed in a Perspective by Dr Andrea Devaney who concludes that this generic drug can be used safely 'in a controlled environment' by a renal pharmacy transplants team to 'avoid inadvertent tacrolimus brand switching' and that 'patient education and awareness is paramount'. I would like to personally encourage our readers to submit other manuscripts that describe the roles of both hospital and clinical pharmacists as well as patient education and awareness in the safe and effective use of follow-on pharmaceutical products. Active participation of all 'stakeholders' is likely to be needed to maximize the risk/benefit of pharmaceutical products.

Finally, modified drug delivery products promise to complicate the approval of otherwise 'simple' generic drug products. A final news article from Dr Christoph Baumgärtel suggests that EMA will soon issue the new EU guidance for the evaluation of medicinal products with modified drug release. I would encourage readers to submit manuscripts covering this important aspect of generic drugs as well as the topics of biosimilars and NBCDs.

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