INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL
REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

E7 Studies in Support of Special Populations: Geriatrics

Questions & Answers

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In order to facilitate the implementation of the E7 guideline, the ICH Experts have developed a series of Q&As:

E7 Q&As

Document History

Code	History	Date
E7 Q&As	Approval by the ICH Steering Committee under *Step 2*	18 September 2009

E7 Geriatric Studies : Questions and Answers

Date of Approval		Questions	Answers
1	**Sept. 2009**	Why do we need an adequate representation of geriatric patients in the clinical database?	Geriatric patients can respond differently from non-geriatric patients to drug therapy in a number of ways: a) The geriatric population has age-related physiological changes that could affect the pharmacokinetics and pharmacodynamics of the drug, and thus can influence drug response. b) These patients often have co-morbidities and concomitant therapies that could interact with the investigational drug and make them more prone to adverse effects. These adverse effects could be more severe and have more serious consequences than in the non-geriatric population. With the increasing prevalence of the geriatric population (elderly and very elderly, i.e., over 75 years) and in view of the recent advances in the scientific field since the ICH E7 guideline was established in 1993, the importance of geriatric data (including the very elderly) in a drug evaluation program has increased. Not all potential differences in pharmacokinetics, pharmacodynamics, disease-drug, drug-drug interactions and clinical response that can occur in the geriatric population can be predicted from non-geriatric populations. Therefore, an appropriate representation of geriatric patients is called for to assess the benefit/risk balance of a drug to be used in this population.
2	**Sept. 2009**	What should be taken into account when estimating an adequate representation of geriatric patients to be included in the clinical database?	It is very important to ensure, to the extent possible, that the population included in the clinical development program is representative of the target patient population. As stated in the current ICH E7 guideline, estimates of the prevalence of the disease to be treated by age or examination of the age distribution of usage for other drugs of the same class or for the same indication, should be provided by the applicant. This will indicate the expected use of the drug and should influence the number of geriatric patients to be included in the marketing application. The current guideline states, “for drugs used in diseases not unique to,

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			but present in the elderly, a minimum of 100 patients would usually allow detection of clinically important differences". Given the increasing prevalence and the growing recognition of the complexity of the geriatric population, because of concomitant therapies and co-morbidities, it might be appropriate to include more than 100 geriatric patients in the Phase II and III database. Patients over the entire spectrum of the geriatric patient population, especially the very elderly, should be included. In the marketing application, data should be presented for patients aged 65 to 74 and for the very elderly patients aged 75 and older to assess the consistency of the treatment effect and safety profile in these patients with the non-geriatric patient population.
3	**Sept. 2009**	Are there any special patient populations or characteristics that are particularly important to address in the planning of the clinical development program?	Geriatric patients often have co-morbidities and concomitant therapies that could interact with the investigational drug and make them more prone to undesirable effects and interactions. Therefore, it is important to assess the safety and efficacy of a drug in these patients, and the inclusion/exclusion criteria of a study should allow their participation. This applies both to drugs intended for the geriatric patient population and for drugs used in diseases present in, but not unique to, the geriatric population.
4	**Sept. 2009**	What should be considered for the clinical development program to adequately characterize the safety and efficacy of a drug for a marketing application?	An appropriate representation of the geriatric population (including patients with concomitant therapies and co-morbidities) should be enrolled in the clinical development program to adequately characterize efficacy and safety in the geriatric population and allow for comparisons with the non-geriatric population. In general it is preferable to include both non-geriatric and geriatric patients in the same study(ies), which can facilitate observation of age-related differences. This information would ordinarily be expected in a marketing application.

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			Every effort should be made to include geriatric patients with concomitant therapies and co-morbidities in the premarketing clinical development program. In some cases, enrolment of these patients can be challenging and it could be appropriate to collect data postmarketing. However, the adequacy of, and the need for, data in these patients should be considered during drug development and discussed in the marketing application submission. Where enrolment of geriatric patients has been insufficient despite the efforts of the applicant, a specific plan to collect data post-marketing should be discussed during development and presented in the marketing application. Information relevant to the geriatric patient population, including any limitations, should be reflected in the product labeling.
5	**Sept. 2009**	Are there concerns related to the data specific to the geriatric population that could be considered in the planning of the clinical studies?	Depending on the mechanism of action of the drug and/or the characteristics of the disease, certain specific adverse events should be looked for in the geriatric population, e.g. effects on cognitive function, urinary incontinence or retention, weight loss, sarcopenia, effects on balance and falls. This can call for specific testing, e.g. for cognitive function. Applicants should also refer to disease specific guidelines for specific recommendations concerning geriatric patients.
6	**Sept. 2009**	In light of recent advances in the field of pharmacokinetics and assessment of drug-drug interactions since the ICH E7 guideline was established, what studies should be considered when developing a drug that will be used in geriatric patients?	The pharmacokinetics in geriatric patients (including the very elderly) should be evaluated to identify age-related differences that are not explained by other factors such as reduced renal function or weight differences. The potential influence of impaired renal/hepatic function as well as potential drug interactions is often assessed in studies with non-geriatric subjects and is addressed in region-specific guidelines that applicants should consider. Population pharmacokinetic analysis could provide the requested data if a sufficient number of patients in different age ranges (including patients >65 and >75 years) are included in the clinical trials. The applicability of

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			population pharmacokinetics is dependent on several factors, e.g. the pharmacokinetics of the drugs, dosing regimens and analytical requirements. A specific pharmacokinetic study comparing non-geriatric and geriatric subjects in the same study (matched for relevant covariates, e.g. height, weight, sex) could achieve the same goals. A single-dose design is usually adequate for drugs with linear pharmacokinetics. A steady state study is, however, recommended for drugs with non-linearity in the pharmacokinetics.