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ICH Guidelines- "E" Series (Efficacy Guidelines) -A Review

K. Bhavyasri*[1], R. Sai Chandana[2], M. Sumakanth[3] and D. Rambabu[4]
[*1, 2, 3] RBVRR Women's College of Pharmacy, Hyderabad.
[4]Gland Pharma Pvt Ltd.

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***Corresponding Author Email:** bhavya.khagga@gmail.com

Abstract

***ICH**-International conference on harmonization of technical requirements for registration of pharmaceuticals for human use is a joint initiative involving both regulatory and research based industry representatives of Europe, Japan and US in scientific and technical discussions of the testing procedure which is required to assess and ensure the efficacy, quality and safety of medicines. The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials in human subject like dose response studies, good clinical practices (GLP). It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics / pharmacogenomics techniques to produce better targeted medicines.*

Keywords
Harmonization, efficacy, good clinical practice.

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E1- CLINICAL SAFETY FOR DRUGS USED IN LONG TERM TREATMENT

The objective of this guideline is to present an accepted set of principles for the safety evaluation of drugs intended for the long-term treatment (chronic or repeated intermittent use for longer than 6 months) of non-life-threatening diseases. For the purpose of this guideline, it is useful to distinguish between clinical data on adverse drug events (ADEs) derived from studies of shorter duration of exposure and data from studies of longer duration, which frequently are non-concurrently controlled studies. It is expected that short-term event rates (cumulative 3-month incidence of about 1%) will be well characterized. Events where the rate of occurrence changes over a longer period of time may need to be characterized depending on their severity and importance to the risk-benefit assessment of the drug. The safety evaluation during clinical drug development is not expected to characterize rare adverse events, for example, those occurring in less than 1 in 1000 patient.[1]

E2A-E2F PHARMACOVIGILENCE

E2A-clinical safety data management: definition and standards for expedited reporting: Deals with the clinical safety data management. It is important to harmonize the way to gather and, if necessary, to take action on important clinical safety information arising during clinical development. Thus, agreed definitions and terminology, as well as procedures, will ensure uniform Good Clinical Practice standards in this area. The initiatives already undertaken for

marketed medicines through the CIOMS-1 and CIOMS-2 Working Groups on expedited (alert) reports and periodic safety update reporting, respectively are important precedents and models.[2]

E2B(R3) clinical safety data management: data elements for transmission of individual case safety reports: Priorities; the following activities have been identified like establishment of an ICH mailbox to receive implementation queries for which the ICH E2B(R3) IWG will prepare responses, finalization of a Change Control Process for documents in the Implementation Guide (IG) package, maintenance of technical documents related to E2B(R3),monitoring of regional implementations and the need to address potential inconsistencies in messages, definition of E2B(R3) codes as needed, to obtain term and identifier lists from Maintenance Organizations (MOs), apply, and maintain any necessary constraints consistent with E2B(R3) requirements, to create initial documentation for use of IDs / terms referenced in E2B (R3) IG.[3]

E2C (R2)-Periodic benefit risk evaluation report: The Periodic Benefit-Risk Evaluation Report (PBRER) described in this Guideline is intended to be a common standard for periodic benefit-risk evaluation reporting on marketed products (including approved drugs that are under further study) among the ICH regions. This Guideline defines the recommended format and content of a PBRER and provides an outline of points to be considered in its preparation and submission.[4]

E2D-Post approval safety data management: definitions and standards for expedited reporting: It is important to establish an internationally standardized procedure in order to improve the quality of post-approval safety information and to harmonize the way of gathering and reporting information. This guideline is based on the content of ICH E2A guideline, with consideration as to how the terms and definitions can be applied in the post-approval phase of the product life cycle.[5]

E2E-Pharmacovigilence planning: This guideline is intended to aid in planning Pharmacovigilance activities, especially in preparation for the early post marketing period of a new drug (in this guideline, the term “drug” denotes chemical entities, biotechnology-derived products, and vaccines). The main focus of this guideline is on a Safety Specification and Pharmacovigilance Plan that might be submitted at the time of license application. The guideline can be used by sponsors to develop a stand-alone document for regions that prefer this approach or to provide guidance on incorporation of elements of the Safety Specification and Pharmacovigilance Plan into the Common Technical Document (CTD).[6]

E2F-Development safety update report: The Development Safety Update Report (DSUR) proposed in this guideline is intended to be a common standard for periodic reporting on drugs under development (including marketed drugs that are under further study) among the ICH regions. US and EU regulators consider that the DSUR, submitted annually, would meet national and regional requirements currently met by the US IND Annual Report and the EU Annual Safety Report, respectively, and can therefore take the place of these existing reports. This guideline defines the recommended content and format of a DSUR and provides an outline of points to be considered in its preparation and submission.[7]

E3-CLINICAL STUDY REPORT

The objective of this guideline is to allow the compilation of a single core clinical study report acceptable to all regulatory authorities of the ICH regions. The clinical study report described in this guideline is an "integrated" full report of an individual study of any therapeutic, prophylactic or diagnostic agent (referred to herein as drug or treatment) conducted in patients, in which the clinical and statistical description, presentations, and analyses are integrated into a single report, incorporating tables and figures into the main text of the report, or at the end of the text, and with appendices containing the protocol, sample case report forms, investigator related information, information related to the test drugs/ investigational products including active control/ comparators, technical statistical documentation, related publications, patient data listings, and technical statistical details such as derivations, computations, analyses, and computer output etc.[8]

E4-DOSE RESPONSE INFORMATION TO SUPPORT DRUG REGISTRATION

Knowledge of the relationships among dose, drug-concentration in blood, and clinical response (effectiveness and undesirable effects) is important for the safe and effective use of drugs in individual patients. This information can help identify an appropriate starting dose, the best way to adjust dosage to the needs of a particular patient, and a dose beyond which increases would be unlikely to provide added benefit or would produce unacceptable side effects. Dose-concentration, concentration - and/ or dose response information is used to prepare dosage and administration instructions in product labeling. In addition, knowledge of dose-response may provide an

economical approach to global drug development, by enabling multiple regulatory agencies to make approval decisions from a common database.[9]

E5-ETHNIC FACTORS IN THE ACCEPTABILITY OF FOREIGN CLINICAL DATA

This guidance is based on the premise that it is not necessary to repeat the entire clinical drug development program in the new region and is intended to recommend strategies for accepting foreign clinical data as full or partial support for approval of an application in a new region. It is critical to appreciate that this guidance is not intended to alter the data requirements for registration in the new region; it seeks to recommend when these data requirements may be satisfied with foreign clinical data. All data in the clinical data package, including foreign data, should meet the 1 Ethnic Factors in the Acceptability of Foreign Clinical Data standards of the new region with respect to study design and conduct and the available data should satisfy the regulatory requirements in the new region. Additional studies conducted in any region may be required by the new region to complete the clinical data package.[10]

E6-GOOD CLINICAL PRACTICE

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible. The objective of this ICH GCP Guideline is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions. The guideline was developed with consideration of the current good clinical practices of the European Union, Japan, and the United States, as well as those of Australia, Canada, the Nordic countries and the World Health Organization (WHO). This guideline should be followed when generating clinical trial data that are intended to be submitted to regulatory authorities. The principles established in this guideline may also be applied to other clinical investigations that may have an impact on the safety and well-being of human subjects.[11]

E7-CLINICAL TRAILS IN GERIATRIC POPULATION

Drugs should be studied in all age groups, including the elderly, for which they will have significant utility. Patients entering clinical trials should be reasonably representative of the population that will be later treated by the drug. The use of drugs in this population requires special consideration due to the frequent occurrence of underlying diseases, concomitant drug therapy and the consequent risk of drug interaction. This guideline is directed principally toward new molecular Entities that are likely to have significant use in the elderly, either because the disease intended to be treated is characteristically a disease of aging (e.g., Alzheimer's disease) or because the population to be treated is known to include substantial numbers of geriatric patients (e.g., hypertension).[12]

E8-GENERAL CONSIDERATION FOR CLINICAL TRAILS

The ICH document "General Considerations for Clinical Trials" is intended to describe internationally accepted principles and practices in the conduct of both individual clinical trials and overall development strategy for new medicinal products. It facilitates the evaluation and acceptance of foreign clinical trial data by promoting common understanding of general principles, general approaches and the definition of relevant terms. It represents an overview of the ICH clinical safety and efficacy documents and facilitates the user's access to guidance pertinent to clinical trials within these documents. It provides a separate glossary of terms used in the ICH clinical safety and efficacy related documents that pertain to clinical trials and indicate which documents contain them.[13]

E9-STATISTICAL PRINCIPLES FOR CLINICAL TRAILS

The focus of this guidance is on statistical principles. This guidance should be of interest to individuals from a broad range of scientific disciplines. However, it is assumed that the actual responsibility for all statistical work associated with clinical trials will lie with an appropriately qualified and experienced statistician, as indicated in ICH E6. The role and responsibility of the trial statistician in collaboration with other clinical trial professionals, is to ensure that statistical principles are applied appropriately in clinical trials supporting drug development. Thus, the trial statistician should have a combination of education/training and experience sufficient to implement the principles articulated in this guidance.[14]

E10-CHOICE OF CONTROL GROUP IN CLINICAL TRAILS

The choice of control group is always a critical decision in designing a clinical trial. That choice affects the inferences that can be drawn from the trial, the ethical acceptability of the trial, the degree to which bias in conducting and analyzing the study can be minimized, the types of subjects that can be

recruited and the pace of recruitment, the kind of endpoints that can be studied, the public and scientific credibility of the results, the acceptability of the results by regulatory authorities, and many other features of the study, its conduct, and its interpretation. The purpose of this guideline is to describe the general principles involved in choosing a control group for clinical trials intended to demonstrate the efficacy of a treatment and to discuss related trial design and conduct issues. This guideline does not address the regulatory requirements in any region, but describes what trials using each design can demonstrate. The choice of the control group should be considered in the context of available standard therapies, the adequacy of the evidence to support the chosen design, and ethical considerations.[15]

E11-CLINICAL TRAILS IN PEDIATRIC POPULATION

The number of medicinal products currently labeled for pediatric use is limited. The goal of this guidance is to encourage and facilitate timely pediatric medicinal product development internationally. The guidance provides an outline of critical issues in pediatric drug development and approaches to the safe, efficient, and ethical study of medicinal products in the pediatric population. Pediatric patients should be given medicines that have been appropriately evaluated for their use. Safe and effective pharmacotherapy in pediatric patients requires the timely development of information on the proper use of medicinal products in pediatric patients of various ages and, often, the development of pediatric formulations of those products. Advances in formulation chemistry and in pediatric study design will help facilitate the development of medicinal products for pediatric use. Drug development programs should usually include the pediatric patient population when a product is being developed for a disease or condition in adults and it is anticipated the product will be used in the pediatric population. Obtaining knowledge of the effects of medicinal products in pediatric patients is an important goal. However, this should be done without compromising the well-being of pediatric patients participating in clinical studies. This responsibility is shared by companies, regulatory authorities, health professionals, and society as a whole.

E11(R1)-clinical investigation of medicinal products in the pediatric population: has evolved since the original ICH E11 Guideline (2000), requiring consideration of regulatory and scientific advances relevant to pediatric populations. This addendum does not alter the scope of the original guideline which outlines an approach to the safe, efficient, and ethical study of medicinal products in the pediatric population. The purpose of this addendum is to complement and provide clarification and current regulatory perspective on topics in pediatric drug development.[16]

E11A-Pediatric exploitation: Pediatric extrapolation has been based on the assumption that there is a sufficient similarity in disease and response to therapy between adult and pediatric patients to allow for collection of different level of evidence to support approval of a product for use in pediatrics. Also, it has generally been required that additional dosing and safety information always be collected. With increased knowledge and understanding, there have been refinements in application of extrapolation in pediatric drug development over the last 20 years. There is now more scientific and regulatory experience on the use of pediatric extrapolation. For example, the uncertainties in the similarity in disease and response to therapy between the source and target population can be viewed as a continuum rather than a specific, sufficient level that must be achieved. These uncertainties affect the confidence in assumptions made in a pediatric extrapolation plan. The availability of existing data affects the degree of uncertainty and confidence in these assumptions. Additionally, the generation of additional data in any proposed pediatric studies should address the uncertainties and confidence in these assumptions. Quantitative approaches to the review of existing data as well as the data that need to be generated are critical in increasing the success of drug development programs because these approaches maximize the use of existing data, increase the efficiency of development programs, and limit the number of children required for enrollment in clinical trials. This guideline would address these approaches that can provide the basis for regulatory decision making. An expert working group (EWG) was formed to revise the ICH E11 guideline, Clinical Investigation of Medicinal Products in the Pediatric Population in 2014. E11(R1) has recently achieved Step 4, and has been adopted as a final guideline by the ICH assembly. This revision includes a high level discussion of pediatric extrapolation, but a more comprehensive discussion of pediatric extrapolation is beyond the scope of the current revision. The E11 (R1) EWG is fully supportive of a separate guideline (e.g., E11A: Pediatric Extrapolation) to provide more specific and detailed guidance about the use of pediatric extrapolation in pediatric drug development.[17]

E12-PRINCIPLES FOR CLINICAL EVALUATION OF NEW ANTIHYPERTENSIVE DRUGS

This document provides general principles for the clinical evaluation of new antihypertensive drugs. It describes core principles for the evaluation of antihypertensive that are accepted in the three ICH regions, but some region-specific differences remain. These differences may be harmonized in future, but it is important at present to refer to existing regional guidelines and to discuss the specific requirements with regional regulatory authorities, if required. This document should be considered together with a number of pertinent ICH guidelines (E1-E10). There are, in addition, existing regional guidelines or draft guidelines i.e. CPMP: Note for Guidance on Clinical Investigation of Medical Products in the Treatment of Hypertension, FDA: Proposed Guidelines for the Clinical Evaluation of Antihypertensive Drugs and MHW: Guideline for the Clinical Evaluation of Antihypertensive Agents. The primary basis of assessment of efficacy of antihypertensive drugs is the effect of the drug on systolic and diastolic blood pressures. In the past the primary endpoint of most studies was diastolic blood pressure. Although all drugs to date have reduced both systolic and diastolic blood pressures, the recognition of isolated or predominant systolic hypertension as a significant and remediable risk factor demands explicit evaluation of the effect of a drug on systolic blood pressure. Many clinical trials of many interventions (including low and high dose diuretics, reserpine, and beta blockers, usually as part of combination therapy) have shown consistent beneficial effects on long-term mortality and morbidity, most clearly on stroke and less consistently on cardiovascular events. Whether some drugs or combinations have 1 Principles for Clinical Evaluation of New Antihypertensive Drugs better effects than others on overall outcomes or on particular outcomes is not yet known. Formal mortality and morbidity outcome studies are not ordinarily required for approval of antihypertensive drugs and the kind of active control mortality and morbidity studies that would be convincing is not well defined. Results of a large number of on-going outcome studies could affect this policy and modify requirements. It should be noted that, even if an antihypertensive effect has been proven, a significant concern about a detrimental effect on mortality and/or cardiovascular morbidity might lead to a need for outcome studies.[18]

E14-CLINICAL EVALUATION OF QT/QTc INTERVAL PROLONGATION AND PROARRHYTHMIC PTENTIAL FOR NON-ARRHYTHMIC DRUGS

This document provides recommendations to sponsors concerning the design, conduct, analysis, and interpretation of clinical studies to assess the potential of a drug to delay cardiac repolarization. This assessment should include testing the effects of new agents on the QT/QTc interval as well as the collection of cardiovascular adverse events. The investigational approach used for a particular drug should be individualized, depending on the pharmacodynamics, pharmacokinetic, and safety characteristics of the product, as well as on its proposed clinical use. The assessment of the effects of drugs on cardiac repolarization is the subject of active investigation. When additional data (non-clinical and clinical) are accumulated in the future, this document may be re-evaluated and revised. The recommendations contained in this document are generally applicable to new drugs having systemic bioavailability, but may not apply to products with highly localized distribution and those administered topically and not absorbed. The focus is on agents being developed for uses other than the control of arrhythmias, as antiarrhythmic drugs can prolong the QT/QTc interval as a part of their mechanism of clinical efficacy. While this document is concerned primarily with the development of novel agents, the recommendations might also be applicable to approved drugs when a new dose or route of administration is being developed that results in significantly higher exposure (i.e., Cmax or AUC). Additional ECG data might also be considered appropriate if a new indication or patient population were being pursued. The evaluation of the effect of a drug on the QT interval would also be considered important if the drug or members of its chemical or pharmacological class have been associated with QT/QTc interval prolongation, TdP, or sudden cardiac death during post-marketing surveillance.[19]

E15-DEFINITIONS FOR GENOMIC BIOMARKERS, PHARMACOGENOMICS, PHARMACOGENETICS, GENOMIC DATA AND SAMPLE CODING CATEGORIES

In order to develop harmonized approaches to drug regulation, it is important to ensure that consistent definitions of terminology are being applied across all constituents of the International Conference on Harmonization (ICH). An agreement on definitions will facilitate the integration of the discipline of pharmacogenomics and pharmacogenetics into global drug development and approval processes. Pharmacogenomics and pharmacogenetics have the potential to improve the discovery, development and

use of medicines. Each of the ICH regions has published specific pharmacogenomic and pharmacogenetic guidelines, or concept papers, and is in the process of developing others. However, the lack of consistently applied definitions to commonly used terminology raises the potential for either conflicting use of terms in regulatory documentation and guidelines, or, inconsistent interpretation by regulatory authorities, ethics committees and sponsor companies. This guideline contains definitions of key terms in the discipline of pharmacogenomics and pharmacogenetics, namely genomic biomarkers, pharmacogenomics, pharmacogenetics and genomic data and sample coding categories. The definition of what constitutes a genomic biomarker is key to understanding the definitions of pharmacogenomics and pharmacogenetics and is therefore introduced in this guideline first. Additional information useful to an understanding of aspects covered by each of the definitions is also provided. Some of the principles described in this guideline might be applicable to proteomics, metabalomics and other related disciplines.[20]

E16-QUALIFICATION OF GENOMIC BIOMARKERS

The use of biomarkers has the potential to facilitate the availability of safer and more effective drug or biotechnology products, to guide dose selection and to enhance their benefit-risk profile. This guideline is based on previous experiences with submissions containing biomarker data in the various regions. These submissions have been either stand-alone biomarker qualification applications or a component of medicinal product related regulatory process marketing applications (NDAs / BLAs / MAAs). The development of a consistent format for submission of biomarker data will facilitate easy review and exchange of assessments between regions. The guideline describes recommendations regarding context, structure and format of regulatory submissions for qualification of genomic biomarkers (as defined in ICH E151). Qualification is a conclusion that, within the stated context of use, the results of assessment with a biomarker can be relied upon to adequately reflect a biological process, response or event, and support use of the biomarker during drug or biotechnology product development, ranging from discovery through post-approval. A biomarker qualification application might be submitted to regulatory authorities if the biomarker directly or indirectly helps in regulatory decision-making. The objective of the guideline is to create a harmonized recommended structure for biomarker qualification applications that will foster consistency of applications across regions and facilitate discussions with and among regulatory authorities. It will also reduce the burden on sponsors as a harmonized format will be recommended for use across all ICH regulatory regions. It is also expected that the proposed document format will facilitate incorporation of biomarker data into specific product-related applications. Biomarker qualification can take place at any time during drug or biotechnology product development, ranging from discovery through post-approval. For those instances where it is appropriate, general guidance for inclusion of biomarker qualification data into the Common Technical Document for the Registration of Pharmaceuticals for Human Use (CTD) format marketing authorization applications are provided in this document. The use of the CTD format would be considered appropriate when biomarker data are submitted as part of an NDA, a BLA, a MAA, other post-approval regulatory procedures or upon request by the regulatory authorities.[21]

E17-GENERAL PRINCIPLES FOR PLANNING AND DESIGN OF MULTI-REGIONAL CLINICAL TRIALS

With the increasing globalization of drug development, it has become important that data from multi-regional clinical trials (MRCTs) can be accepted by regulatory authorities across regions and countries as the primary source of evidence, to support marketing approval of drugs (medicinal products). The purpose of this guideline is to describe general principles for the planning and design of MRCTs with the aim of increasing the acceptability of MRCTs in global regulatory submissions. The guideline addresses strategic programme issues as well as issues that are specific to the planning and design of confirmatory MRCTs, and it should be used together with other ICH guidelines, including E5, E6, E8, E9, E10, and E18. In the era of globalization of drug development, it may be challenging to conduct a drug development programme globally, in part due to distinct and sometimes conflicting requirements from regulatory authorities. At the same time, regulatory authorities face increasing challenges in evaluating data from MRCTs for drug approval. Data from MRCTs are often submitted to multiple regulatory authorities without a previously harmonized regulatory view on the development programme. There are currently no ICH guidelines that deal specifically with the planning and design of MRCTs, although the ICH E5 guideline covers issues relating to the bridging of results from one region to another. MRCTs conducted according to the present guideline will allow investigation of treatment effects including safety evaluations in the overall population

as well as investigations of the potential impact of intrinsic and extrinsic factors (described as ethnic factors in the ICH E5 guideline) on the treatment effect. MRCTs, which are properly designed and executed according to this guideline, may facilitate more efficient drug development and increase the possibility of submitting marketing authorization applications to multiple regulatory authorities in different regions simultaneously, thus providing earlier access to new drugs worldwide. In addition, MRCTs conducted according to the present guideline may enhance scientific knowledge about how treatment effects vary across regions and populations under the umbrella of a single study protocol, and how this variation may be explained by intrinsic and extrinsic factors. MRCT is defined in the present guideline as a clinical trial conducted in more than one region under a single protocol. In this context, a region may refer to a geographical region, country or regulatory region. The primary focus of this guideline is on MRCTs designed to provide data that will be submitted to multiple regulatory authorities for drug approval (including approval of additional indications, new formulations and new dosing regimens) and for studies conducted to satisfy post-marketing requirements. Certain aspects of this guideline may also be relevant to studies conducted early in clinical development or in later phases. The present guideline mainly covers drugs including biological products, although some sections may not be applicable to all development programmes (e.g., pharmacokinetics not used for preventive vaccine dose-finding).[22]

E18-GENOMIC SAMPLING AND MANAGEMENT OF GENOMIC DATA

The main objective of this guideline is to provide harmonized principles of genomic sampling and management of genomic data in clinical studies. This guideline will facilitate the implementation of genomic studies by enabling a common understanding of critical parameters for the unbiased collection, storage, and optimal use of genomic samples and data. This guideline also intends to increase awareness and provide a reminder regarding subjects' privacy, protection of the data generated, the need to obtain suitable informed consent, and the need to consider transparency of findings in line with local legislation and regulations. This guideline is intended to foster interactions amongst stakeholders, including drug developers, investigators and regulators, and to encourage genomic research within clinical studies. Genomic research could be used in all phases of drug development to assess genomic correlates of drug response, and to understand mechanisms of disease or drug pharmacology. The identification of genomic biomarkers underlying variability in drug response may be valuable to optimize patient therapy, design more efficient studies, and inform drug labeling. Furthermore, the generation and interpretation of genomic data, both within and across clinical studies and drug development programs, allow for a better understanding of pharmacological and pathological mechanisms and enable the identification of new drug targets. Regulatory agencies in the ICH regions have independently published guidelines encouraging genomic sample collection throughout the life cycle of a drug. The lack of a harmonized ICH guideline on genomic sampling and data management from clinical studies makes it difficult for sponsors and researchers to collect genomic samples and conduct genomic research in a consistent manner in global clinical studies. Genomic samples may be used for a variety of analyses, including single genes, sets of genes and the whole genome, which may or may not be pre-specified in the clinical study objectives at the time of collection. The scope of this guideline pertains to genomic sampling and management of genomic data obtained from interventional and non-interventional clinical studies. Genomic research can be conducted during or after a clinical study. It may or may not be pre-specified in the clinical protocol. This document addresses use of genomic samples and data irrespective of the timing of analyses and both pre-specified and non-pre-specified use. Genomic samples and data described in this guideline are consistent with the deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) characteristics defined in ICH E151. The focus of this guideline is on the general principles of collection, processing, transport, storage, and disposition of genomic samples or data, within the scope of an informed consent. Technical aspects are also discussed when appropriate, recognizing the rapidly evolving technological advances in genomic sampling and data generation. No detailed guidance is included on bio banking regulations or ethical aspects, as these are governed by the principles of the Declaration of Helsinki and national rules and regulations.[23]

E19-SAFETY DATA COLLECTION

This guideline is proposed to provide internationally harmonized guidance on when it would be appropriate to use a targeted approach to safety data collection in some late-stage pre-marketing or post-marketing studies, and how such an approach would be implemented. Specifically, in the later stages of drug development, when the common side

effects of a drug are well-understood and documented, a more targeted approach to safety data collection may be appropriate, as long as patient welfare is not compromised. Under such circumstances, some of the data routinely collected in clinical studies may provide only limited additional knowledge. These data may include: non-serious adverse events, routine laboratory assessments, physical examinations, vital signs, and concomitant medications. By tailoring safety data collection in some circumstances, the burden to patients would be reduced, a larger number of informative clinical studies could be carried out with greater efficiency, studies could be conducted with greater global participation, and the public health would be better served. The FDA currently provides guidance for situations where selected data collection may be sufficient. The proposed Guideline would be consistent with risk-based approaches and quality-by-design principles. There is no widely adopted guidance on when the use of targeted safety data collection would be appropriate in late-stage pre-marketing or post-marketing studies, or on how to implement such an approach. Thus, this topic represents an ideal opportunity for international harmonization.[24]

CONCLUSION:

The work carried out by ICH under the Efficacy heading is concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/ genomics techniques to produce better targeted medicines.

REFERENCES:

[1] ICH E1 Guideline: clinical safety for drugs used in long term treatment
[2] ICH E2A Guideline: Clinical safety data management: definitions and standards for expedited reporting
[3] ICH E2B(R3) Guideline: Clinical safety data management: data elements for transmission of individual case safety reports
[4] ICH E2C (R2) Guideline: Periodic benefit risk evaluation report
[5] ICH E2D Guideline: post approval safety data management
[6] ICH E2E Guideline: Pharmacovigilance planning
[7] ICH E2F Guideline: development safety update report
[8] ICH E3 Guideline: structure and content of clinical study reports
[9] ICH E4 Guideline: dose response studies
[10] ICH E5 Guideline: ethic factors
[11] ICH E6 Guideline: good clinical practice
[12] ICH E7 Guideline: clinical trials in geriatric population
[13] ICH E8 Guideline: general consideration for clinical trials
[14] ICH E9 Guideline: statistical principles for clinical trails
[15] ICH E10 Guideline: choice of control group and related issues in clinical trials
[16] ICH E11 (R1) Guideline: clinical investigation of medicinal products in the pediatric population
[17] ICH E11A Guideline: paediatric extrapolation
[18] ICH E12 Guideline: clinical evaluation by therapeutic category
[19] ICH E14 Guideline: clinical evaluation of QT
[20] ICH E15 Guideline: definitions in pharmacogenetics/pharmacogenomics
[21] ICH E16 Guideline: qualification of genomic biomarkers
[22] ICH E17 Guideline: multi regional clinical trials
[23] ICH E18 Guideline: genomic sampling
[24] ICH E19 Guideline; safety data collection