Regulatory Writing

Module 11 Topic 5

Regulatory Affairs versus Writing

RA Managers

Liaison between pharmaceutical company and regulatory bodies

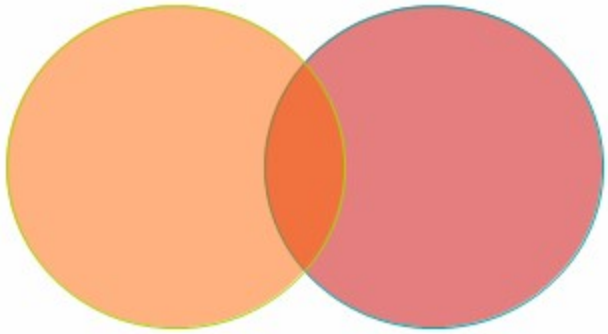
Review

Summarize

Manage project eg, MAA

Guidelines and regulations

Development plans



Overlap

Write Summaries and Overviews Write Investigator Brochures

Write Paediatric Investigation Plans

Writers

Write Clinical Study Reports

Write protocols

Write manuscripts

Regulatory writing

Involves writing documents for regulatory agencies

- Drugs,
- Devices and
- Biologics that are approved and
- Stay approved for marketing to humans

Regulatory documents can be huge and are formulaic

- Clinical study reports
- Clinical study protocol
- Patient informed consent forms
- Investigator brochures
- Summary documents

Some examples of regulatory documents

EU documents	US documents	Nature and purpose
Investigational Medicinal Product Dossier (IMPD)	Investigational New Drug (IND) Application	An application for permission to use an investigational product in a clinical trial with human subjects. A separate IND or IMPD is required for each product used in a trial (including placebo). These documents may need updating for the approval of each new clinical trial, if the known information about an investigational product changes significantly
Investigator's Brochure (IB)	Investigator's Brochure (IB)	A compilation of all the relevant clinical and medicinal data of an investigational new drug or medicinal product, as relevant when studying the medicine in human subjects
Clinical Study Protocol (CSP)	Clinical Study Protocol (CSP)	A document that lays out strict guidelines for the performance of a clinical trial. Based on the most current data about the disease under treatment and the medicine being tested, the protocol lays out guidelines for diagnosis, prognosis, handling of subjects, dosage of medicines and risk/benefit considerations, providing decision options and their expected outcomes
Informed Consent Form (ICF)	Informed Consent Form (ICF)	A document to be signed by all subjects who are to take part in the clinical trial – to confirm that they understand and accept the objectives, methods and risks involved
Paediatric Investigation Plan (PIP)	Pediatric Study Plan (PSP)	A development plan that is required if the investigational product is to be licensed for use in children. It describes how clinical data will be obtained safely in clinical studies with children

Table 1: Documents needed to start a clinical trial

Protocol

Protocol

- A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study.

Contents

- Protocol title and date, name and address of principal investigator, site(s) where study will be performed
- Background/Rationale/Literature Review - basis for doing the clinical research study
- Hypothesis/Key Questions - the hypothesis being evaluated; the key questions being asked in the research study
- Research Objectives and Purpose - an extension of the hypothesis/key questions-, can be combined with them

Research Methods

- Study Design (includes some or all of the following)
- Primary and secondary endpoints
- Type/design of the study (double-blind, placebo-controlled, etc.)
- Measures taken to avoid/minimize bias (randomization, blinding)
- Study treatments or interventions
- Expected duration of subject participation; what is done and when
- Stopping rules or discontinuation criteria

Elements

- Title: identifying number, version and date, amendments if any
- Name and address of sponsor and monitor
- Name and title of person authorized to sign the protocol and amendments
- Name and title (contact details) of the sponsor's medical expert

Elements (contd)

- Name and title of the investigator responsible for conduction the trial along with contact details
- Name and title and contact details of the physician (dentist) responsible for the trial site related decisions.
- Names addresses of clinical laboratory involved in the trial

Background Information

- Name and description of the investigational product
- Summary of relevant non clinical study findings
- Summary of known risks and benefits to humans
- Description of route of administration and dosage schedule

Background

- Statement assuring compliance with ICH – GCP and applicable regulatory requirements
- Description of the population to be studied
- References to literature relevant to the trial

Trial Design

- Scientific integrity and credibility of the trial depend upon the trial design. This should include:
- Primary and secondary endpoints to measured during the trial
- A description of the type/design of the trial to be conducted. Schematic diagram of trial design, procedures and stages

Trial Design

- Methods of :
  - Randomization
  - Blinding
- Trial treatment, dosages, schedules, dosage form, packing and labeling
- Expected duration of the subject participation, with visit schedules etc.
- Stopping rules for individual subjects, parts or the entire trial

Trial Design

- Accountability procedures for the investigational product, comparator and placebo
- Maintenance of trial treatment randomization codes and procedures for code break
- Identification of any data written directly into the CRF (absence of source documents)

Subjects

- Inclusion criteria
- Exclusion criteria
- Withdrawal criteria including reasons, and replacement and follow up of withdrawn subjects

Treatment

- Dose, dosing schedules, etc for the treatment and control groups
- Medications permitted (other than the ones under test) and those not permitted during the trial
- Procedures for monitoring subject compliance

Efficacy and Safety

- Efficacy parameters and methods of assessing the same.
- Safety parameters and methods of assessing the same.
- Procedures for recording and reporting Adverse events
- Type and duration of follow up of adverse events

Statistics

- Statistical methods to be employed
- Statistical calculation for number of subjects reasons of choice and power.
- Level of significance
- Criteria for termination of trial
- Procedures for missing data
- Reporting deviation from original statistical plan
- Selection of subjects for analysis

Other elements

- Quality control and assurance procedures
- Ethics
- Data Handling and record keeping
- Financing and Insurance
- Publication policy
- Supplements

Conclusion

- Protocol is the most important of all clinical trial documents
- It is also the first to be prepared and discussed with the investigators.
- It is a confidential document since it contains most useful information on an investigational drug.

NIH Guidance on Protocol Writing

- Protomechanics:

http://www.cc.nih.gov/ccc/protomechanics/

- The Office of Human Subjects Research:

http://ohsr.od.nih.gov/info/info.html

- The NCI Investigators' Handbook:

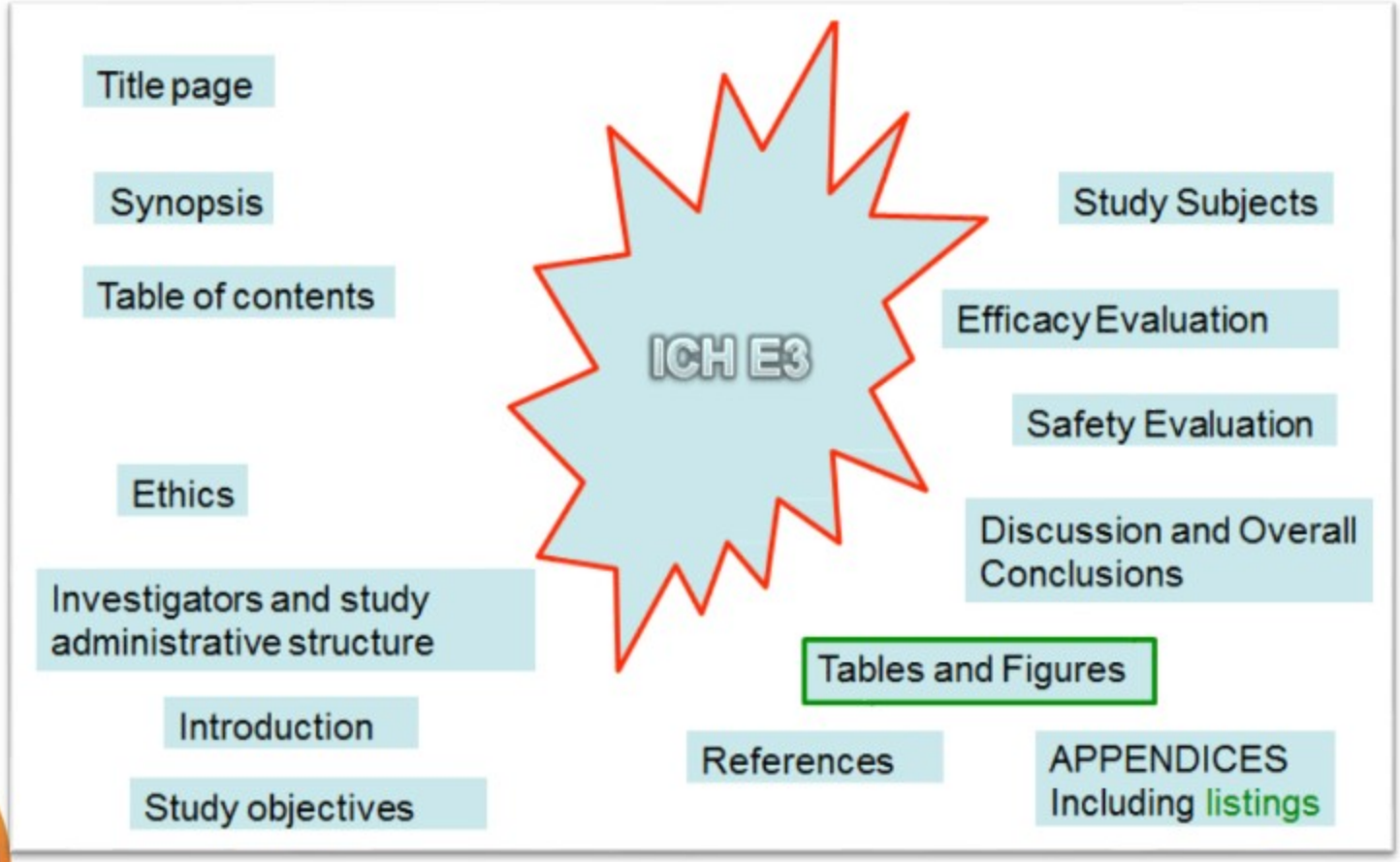
http://ctep.cancer.gov/handbook/index.html

Clinical Study Report

Clinical Study Reports

- CSRs describe the background, rationale, methodology and full results for a clinical study
- Called integrated reports as they cover clinical and statistical aspects
- Guideline ICH E3 on structure and content of CSRs: 53 pages of 'guidance'
- Main text often around 80-200 pages; complete reports with tables and figures plus appendices (including listing of all recorded data) are usually 1000s of pages
- Move over time from all paper to completely electronic reports – which involve 'publishing'
- Elapsed time: 2-12 months; writing time 3-8 weeks

Contents of a CSR

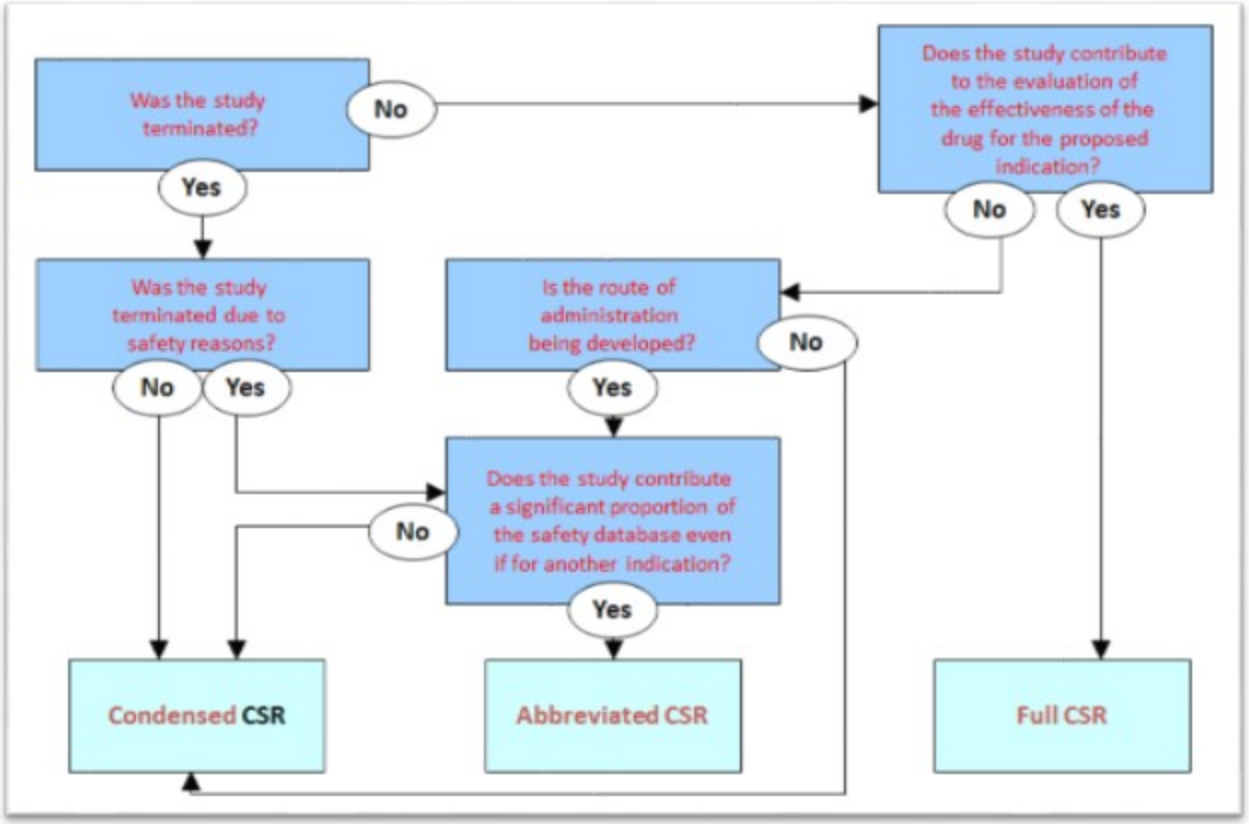


Clinical Study Report

- Types of Clinical Study Reports
  - Full Clinical Study Report (CSR)
  - Abbreviated Clinical Study Report (ACSR)
  - Condensed Clinical Study Report (CCSR)
  - Clinical Pharmacology Study Report (CPSR)

Clinical Study Report Types

- Decision tree for CSR types for clinical studies



The clinical study report (CSR)

- The CSR is the major set piece in a clinical trial
- Built from all data on the drug
- Done in consultation with the statisticians, the clinical team and the medics
- This is the ultimate write-up of an experiment ~ dissertation

The CSR

- Every pre-clinical and clinical study in drug development has to be agreed with the authorities before execution and written up afterwards - as a CSR
- CSRs are the building blocks of a Marketing Authorization Application (MAA)
- http://www.emea.europa.eu/pdfs/human/ich/013795en.pdf

Who writes CSRs

- Medical writing groups within Pharma companies, e.g.: Astra-Zeneca (Alderley Edge), Genzyme (Cambridge)
- Clinical research organisations: multiple
- Specialist companies, e.g.:
  - Constella Group (Milton Park): www.constellagroup.com
  - Insight Medical Writing (Finstock): www.insightmw.com

Investigator's Brochure

Investigator's Brochure

- The Investigator's Brochure is an axis document in a new drug's clinical development programme. Crucial to various processes that regulate clinical research into new drugs, its content is well defined
- The ICH E6 guideline specifies that an Investigator's Brochure should include information on the drug product to be investigated and its performance in non-clinical studies along with specific guidance to investigators on the drugs use
- The Investigator's Brochure is a multidisciplinary document, summarising information from each of the teams involved in a drug's development

IB-Purpose

- To provide information to the Investigator and others involved in a clinical study on such issues the appropriateness of dose, dose frequency/interval and the characteristics of the investigational medicinal product (IMP) – so that it can inform safety considerations and clinical management of study subjects during a clinical trial

Structure of an Investigator's Brochure

- The structure of an Investigator's Brochure structure is defined within ICH E6 (Section 7) [2]:
- Summary
- Introduction
- Physical, chemical, and pharmaceutical properties and formulation
- Non-clinical studies
- Effects in humans
- Summary of data and guidance for the Investigator

Introduction

- Introduction should be 1–2 pages in length and provide a high-level overview of the IMP and the setting of its proposed use
- The introduction should provide a background on the therapeutic rationale behind an IMPs use and its target indication
- It should include the generic name and the tradename of any drug product, its active ingredient(s) and the pharmacological class along with a summary of its position within this class
- The content should reference the scientific literature and incorporate aspects of the IMPs clinical development plan and associated briefing packages

Physical, chemical, and pharmaceutical properties and formulation

- Product code names, information relating to the chemical structure and physical form/solubility of the drug substance relevant to clinical use/formulation
- Qualitative list of all excipients without excipient grades and justification for inclusion of the excipients in the formulation if clinically relevant
- Details of any matching placebos if relevant
- Recommendations on storage and handling of the dosage form. This may be by reference to the product label

Non-clinical studies

- It should report on all relevant non-clinical pharmacology, toxicology, pharmacokinetic and investigational product metabolism studies, reporting on the nature and frequency of effects.
- In addition to summarising the time of onset and duration of any effects and any dose response findings the reports should summarise information:
- Species tested
- Number of sex in each group
- Unit dose (e.g., mg/kg)
- Dosing intervals
- Route of administration
- Duration of dosing

Effects in Humans

If the Investigator's Brochure is intended to support a first-time-in-human study and no clinical studies have yet been conducted this section should be left blank.

- Where clinical studies have been conducted this section should start by noting the stage of development for the IMP and summarise the studies that have been conducted
- A description of each completed clinical trial should be provided; ICH E6 states available information on pharmacokinetics, metabolism, pharmacodynamics, dose response, safety, efficacy and other pharmacological activities should be included [2]

Marketing experience

When the product is not marketed this section is left blank with a statement that the product is not yet marketed.

- Information should be provided on countries where the IMP has been marketed or approved and provide information of any relevant history of use and, if possible, an estimate of patient exposure
- Countries where the investigational product failed to achieve marketing approval/registration or was withdrawn should also be recorded
- Any post-marketing safety information available to the sponsor will also need to be summarized along with information from any pharmacovigilance databases

Summary of data and guidance for the investigator

- This section should provide an overall discussion of the nonclinical and clinical data, and should summarise the information from various sources on different aspects of the investigational product(s), wherever possible
- Where appropriate, the published reports on related products should be discussed
- Practical information is provided for the management of subjects being treated with the investigational product
- Information may also be drawn from published knowledge on other drugs in the same class

References, Supplements and Appendices

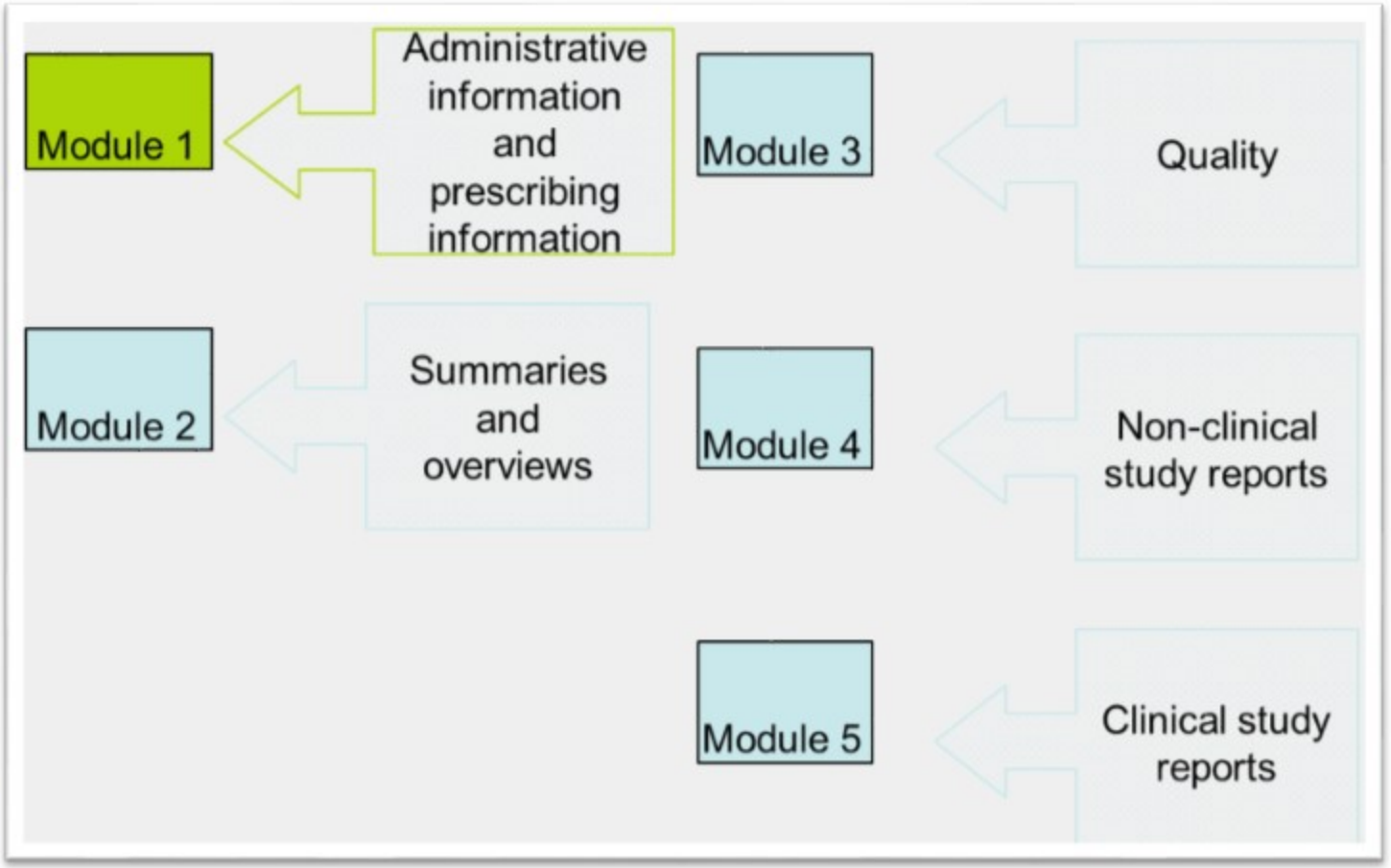
- References may be provided at the end of each section of the document or be given in a combined list at the end of the Investigator's Brochure
- References should not be made to Sponsor documents (as these may not be readily available to an investigator)
- A supplement should be considered as a separate, standalone document and not a revision or an appendix

References, Supplements and Appendices

- A supplement should adopt the format of the parent Investigator's Brochure
- Information provided in a supplement should be fully incorporated into the next revision of the Investigator's Brochure
- Appendices should be provided where additional information to support that summarised in the body of the document could be helpful

The Common Technical Document

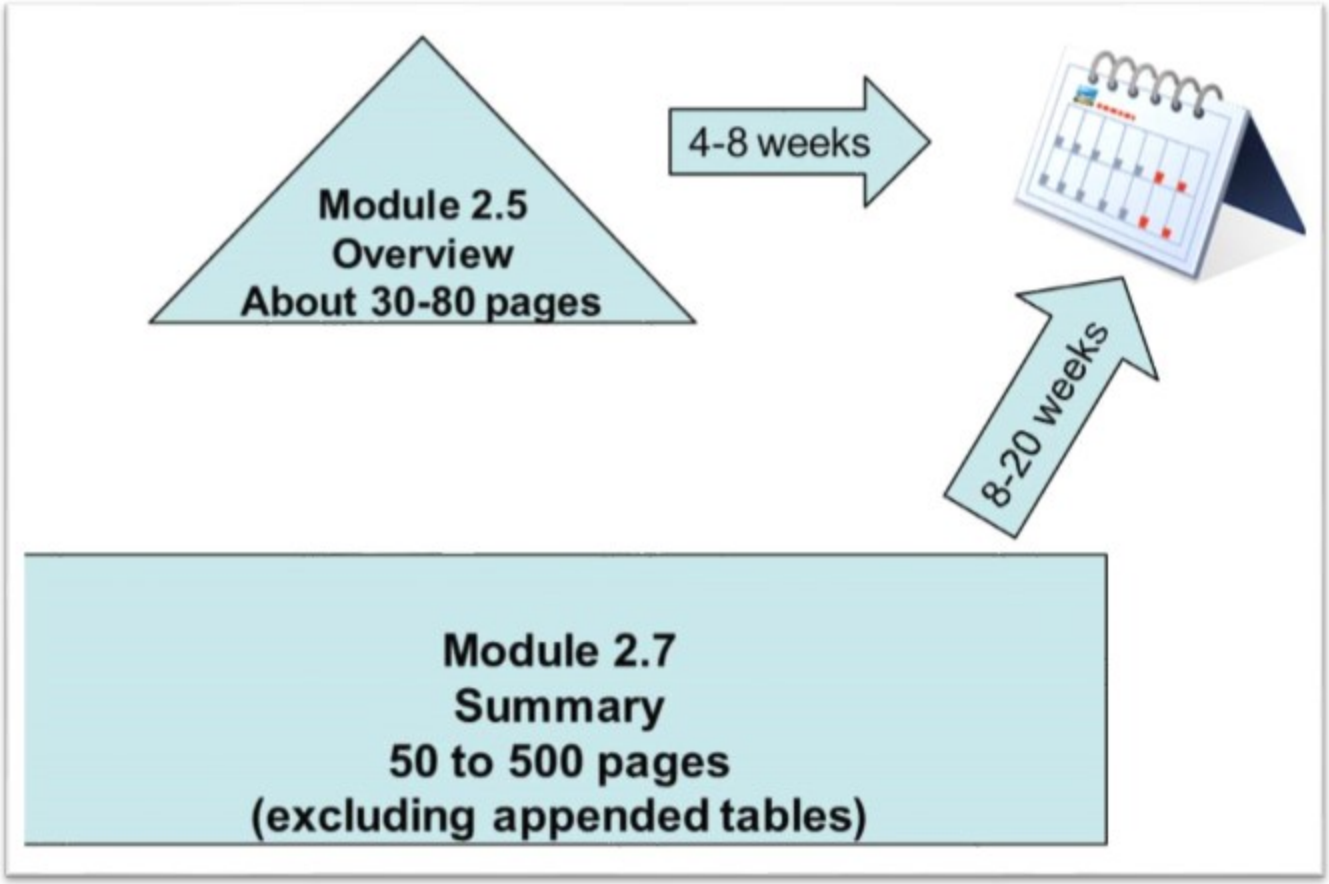
The Common Technical Document



Module 2 Summaries and Overviews

- CTD Table of Contents (Module 2.1)
- CTD Introduction (Module 2.2)
- Quality Overall Summary (Module 2.3)
- Non-clinical Overview (Module 2.4)
- Clinical Overview (Module 2.5)
- Non-clinical Summary (Module 2.6)
- Clinical Summary (Module 2.7)

How Big? How Long?



Module 2.7

- Summary of Biopharmaceutic Studies and Associated Bioanalytical Methods
- Summary of Clinical Pharmacology Studies
- Summary of Clinical Efficacy
- Summary of Clinical Safety
- Literature References
- Synopses of Individual Studies

Module 2.7.3 Summary of Clinical Efficacy

- Background and Overview of Clinical Efficacy
- Summary of Results of Individual Studies
- Comparison and Analyses of Results Across Studies
- Study Populations
- Comparison of Efficacy Results of All Studies
- Comparison of Results in Sub-populations
- Analysis of Clinical Information Relevant to Dosing Recommendations
- Persistence of Efficacy and/or Tolerance Effects
- Appendix

Overviews

Critical analysis of non-clinical and clinical data in CTD
Discussion and interpretation of data

Strengths and limitations of development programme and results
Benefits and risks
How results support prescribing recommendations

EU versus US

Expert input

Module 2.5

- Product Development Rationale
- Overview of Biopharmaceutics
- Overview of Clinical Pharmacology
- Overview of Efficacy
- Overview of Safety
- Benefits and Risks Conclusions
- Literature References

Narrative

Narrative

When you are asked to write a short story, or asked to do some "creative writing", you are doing what is called "Narrative Writing." Narrative writing is meant to entertain! Part of being human is getting to tell great stories!




Examples: Story (personal, true, imaginative), Fable, Myth, Poem,

Play, Biography, and Autobiography

What is a Clinical Narrative?

- A narrative is a small document (100-500 words) that is required by the Food and Drug Administration to briefly describe the events in the life of a subject
- These are required when the subject enrolled in a study or within 30 days of taking study medication discontinued the study because of an adverse event, had 1 or more serious adverse events or died

- Medical narratives are an important part of the reports prepared for any clinical trial
- These are written to provide a brief description of events occurring during the trials
- Narratives can be written as part of the end report on trials or in case of special events where a participant leaves the trial due to severe adverse events

Adverse Event Narratives

- The analysis of adverse events (AEs) is an important component for understanding the safety profile of any new therapy under investigation
- An AE is any unfavorable experience that occurs during the course of a clinical trial that may or may not be due to the particular treatment being administered
- Of particular importance, serious adverse events (SAEs) are AEs that result in death, are life threatening, require inpatient hospitalization or prolongation of hospitalization, result in disability or permanent damage, or are congenital anomalies or birth defects

- When a clinical trial subject has an SAE or other significant adverse event, such as those leading to the discontinuation of the study, a narrative is written for the clinical study report
- These AE narratives summarize the details surrounding the event to enable understanding of the circumstances that may have led to the occurrence and its subsequent management

- Such details may include the dose of study drug at the time of the event, the duration of the dose prior to the event, concomitant medications taken at the time of the event and used to treat the event, and other AEs that may have recently occurred.
- Other details include demography, medical history, lab results, the severity of the event and whether the event was related to study medication

- Narratives are written from the original SAE reports from the clinical site in combination with data listings that are generated as part of the study deliverables
- Information contained in the typical narrative requires the medical writer to review these many disparate data sources
- This is time consuming and, true for any manual effort, can require additional review and quality control

Medical Narratives written at the End of Clinical Trials

- These types of medical narratives are written on successful completion of the clinical trial as a part of the safety reports. This helps in setting guidelines for clinical trials conducted in future

Medical Narratives written during the Ongoing Clinical Trials

- A lot of severe and adverse events may occur while the clinical trials are on-going
- These types of medical narratives are meant to describe all such events
- Adverse and severe events are to be reported through narratives within a deadline and must be completed 3 months prior to the preparation of the final clinical report
- All the events that occur after the deadline are reported through narratives and are included as a part of the data analysis

Medical Narratives written Post-marketing

- The purpose of the narratives written under this category is to take into account the serious and adverse events that were not compiled in the closing results of clinical trials by the safety officer
- There are several events that patients do not report to healthcare professionals and are revealed post-marketing
- There are some patients who do not want to reveal any other drug intake during the trials and thus prefer not to report any events during trials

Source for narratives

- Safety reports are also called CIOMS reports or SAE reports
- Safety reports are written by the Safety Officer or by a writer working under his supervision and are required for any subjects with a serious adverse events which emerged during a clinical trial and also for any patient with serious adverse events that have emerged when taking approved drugs (post-marketing)
- Each time a death or serious adverse event occurs in a subject in a clinical trial or a patient taking the drug after it has been approved, a new report has to be written and filed with the FDA within 15 days

Preferred terms, Investigator Terms and System-Organ Class

- Because the same event occurring in two different people can be recorded differently by different investigators, dictionaries have been devised to group terms together
- The dictionary most widely used is the WHOART dictionary
- The ICD-9 code is a step further, after the terms have been grouped together they are assigned a number. The ICD-9 code was adapted from the WHOART dictionary by the Centers of Disease Control in order to track mortality and morbidity data. The ICD-10 code is becoming the more frequently used coding system

- The Safety Officer, or someone working under his supervision, has the task of taking what the investigator said was the adverse event, and coding this into terms that can be added to databases and sorted in order to find clusters of adverse events that are associated with drug use
- The words the investigator uses are called the Investigator Terms or the **Verbatim** Terms
- The Safety Officer decides which Preferred Term this most approximates. Examples of Investigator Terms are “heart attack” and “myocardial infarction” which are then coded to the Preferred Term “myocardial infarction”

- A further sort of Preferred Terms is made by the Safety Officer who codes Preferred Terms as "**System-Organ-Class**"
- When a verbatim term has been assigned a preferred term, that is the term that is used to describe the event in the tops of the narratives and throughout the clinical study report
- The verbatim term only appears in the body of the narrative and in other documents only when identified as the verbatim term

The Body of the Narrative

- The narrative is a stylized document, with at least **4 paragraphs**
- The number of paragraphs will increase from 4 only if more than 1 serious adverse event emerged during treatment. In the narrative body, the medical reviewer should find enough information to understand what happened and why without having to wade through information that does not lead to his or her understanding of why this event was coded a serious event

The Body of the Narrative

- **The first paragraph:** In the first sentence, explain when the subject was diagnosed with the indication for which he or she is being treated and explain concomitant medications. In the second sentence, list the medical history and previous medical and surgical therapies. Some medical reviewers require all drugs and all previous diseases and injuries to be listed, some reviewers require only drugs, injuries and diseases relevant to the indication and to the event we are reporting

- **The second paragraph:** These sentences discuss the event itself, what happened to the subject before and after and how the investigator handled the event. The first sentence details concisely which study day (in cancer therapy, it will be cycle number and cycle day or study day and cycle number) and what happened in the words of the investigator (do not use preferred terms here). The last sentence explains when and whether the event was resolved and what action the investigator took with the drug.
-

- **The third paragraph:** This paragraph is 1 sentence which lists the medications taken within 2 weeks of the start of the event. Some medical reviewers want all medications and therapies listed, others want only those that are related to the event or related to treating the indication. The medications listed are all listed by generic names, not brand names

- If a second serious adverse event has been reported for the subject within 30 days of the last dose of study medication, the **fourth** and **fifth** paragraphs will copy the second and third paragraphs. Similarly, if a third or fourth serious adverse event has been reported

- **The final paragraph:** This paragraph is 1 sentence describing concisely the severity of each serious adverse event its relatedness to study medication in the words of the investigator. The event is described by Investigator term, is classified by the NCI scale of severity as determined by the investigator and is either unrelated, of unknown relationship, possibly, probably or definitely related to study medication according to the investigator. The information in this paragraph will come out of the safety reports, it should agree with the information in the database

Queries When Writing the Narratives

- If data is missing in the clinical database and in the safety report that prevents the medical writer from writing a complete study, the medical writer should query the clinical research associate assigned to the study
- If the information is not readily available, the clinical trial site or investigator can be queried. The Statisticians can open the clinical database and change some data and redo the listings if the data is very unclean. Both procedures are very expensive, especially the latter, and are not conducted lightly and not without high level approval

Queries When Writing the Narratives (contd)

- If the data in the clinical database has inaccuracies compared with the safety report, or the safety reports have information gaps and different outcomes than the clinical database, the Safety Officer can arrange to update individual safety reports

Narrative Template

- The template will be given directly to individuals who have been trained by Medical Writing in narrative writing
- The font should be Times New Roman. Other style issues, the width of the margins, spaces between lines, wording in each paragraph has been defined in the template and only the template should be used for constructing these narratives

Death: ☐
Serious adverse event: ☒
Discontinuation due to adverse event: ☐
Discontinuation due to laboratory abnormality: ☐

Protocol:	Gxxxxxx
Subject identifier:	Xxxxx
Subject demographics:	75-year-old white male
Treatment group:	Drug p: z mg x y days
Date of first dose of study drug:	29 Mar 2001
Date of last dose of study drug (study day):	05 May 2001 (Day 38)
Preferred term for adverse event:	Renal impairment NOS

Narrative: Subject xxxxxx had cancer (disease needs to be specified), which was diagnosed in Jun 1998. The subject previously received treatment with vincristine, dexamethasone, melphalan, and prednisone. The subject's pertinent medical history included cardiac arrhythmia, myocardial infarction, deep vein thrombosis, hypercholesterolemia, acute renal failure, and hypertension.

On 30 Apr 2001 (Cycle 1, Day 33; 15 days after completing Cycle 1 therapy), the subject was admitted to the hospital for treatment of acute renal insufficiency. The subject complained of a cough one week before admission, and was treated with a dose of pentamidine for *Pneumocystis carinii* pneumonia and reported decreased urine output since that time. A baseline 24-hour urine collection on 14 Mar 2001 revealed 75% lambda light chain Bence-Jones protein, a total protein of 2700 mg/24 hours, and a urine M-protein of 2025 mg/24 hours; the investigator considered that the increase in monoclonal proteins was related to a dental abscess. On 27 Mar 2001, his baseline creatinine was 1.9 mg/dL. On admission, the subject's creatinine was

Narrative Review Process

- Getting from a draft narrative to a narrative report that appears in an appendix to the clinical study report usually involves several review processes
- The first is by the author, the second is by medical reviewers to make sure the narrative makes sense from a medical perspective, the third is by Quality Assurance, to make sure all the pieces fit together and the narrative is accurately represents data from the sources from which it was written

Subject: 101004
Randomized Arm: NIC .15
Investigator: 101A
Drug and Dose at Event Onset: 30 mg/h of NIC .15

Serious Adverse Event (coded term [reported term]): COMA [COMA]

Subject 101004 was a 48-year-old white female. Her medical history included focal deficit (1988), headache (1988), loss of consciousness (1988), vomiting (1988), other medical condition (1977) and allergies (start date unknown). She began dosing with 30 mg/h of nic .15 on 28JAN1988 (Day 1). The subject discontinued the trial on 31JAN1988 (Day 4) due to death.

On 28JAN1988 (Day 1) the subject experienced a coma (severe) which was considered a serious adverse event (SAE). Though the event was considered serious, no reasons were provided on the case report form. At the time of the event, the subject was taking 30 mg/h of nic .15 and had been at this dose for 1 day. The SAE occurred on the first day of dosing with any study medication. Trial medication had an action of drug withdrawn as a result of the event. It is not known from the case report form if therapeutic measures were administered to treat the event.

Adverse events that occurred within a ±3-day window of the onset of the SAE included brain oedema (mild), hydrocephalus (severe), hyperglycaemia (mild), hypotension (severe), intracranial pressure increased (severe), subarachnoid haemorrhage (severe) and vasoconstriction (severe). Concomitant medications taken at the onset of the SAE included docusate sodium (stool softner), phenobarbital (sedative), potassium supplements (fluids) and ranitidine (decrease acidity).

The subject had the following abnormal lab tests at baseline: high creatine kinase [411 U/L, range = (15 - 195)], high chloride [112 mmol/L, range = (97 - 107)], high leukocytes [21 U/L, range = (3 - 20)], low partial pressure carbon dioxide [2394 Pa, range = (4655 - 5985)] and high partial pressure oxygen [31654 Pa, range = (9975 - 13965)]. The subject had no on-study lab tests with results different than baseline on or prior to the start day of the event. On the closest lab test day subsequent to the start of the event , the subject had the following on-study lab tests with results different than baseline: low blood urea nitrogen [2.142 mmol/L, range = (2.499 - 7.497) , BL = normal], low carbon dioxide [91.308 mg/dL, range = (100.004 - 130.44) , BL = normal], low creatinine [0.053040001768 mmol/L, range = (0.05746 - 0.10606) , BL = normal] and normal leukocytes [11 U/L, range = (3 - 20) , BL = high].

The investigator considered the AE to be related to study medication. The final outcome of the event was reported as recovered/resolved on 31JAN1988 (Day 4).

Programmed Patient Narrative

(1st Step at Automation)*

(1) Identification of narrative sections to be programmed

(2) Development and approval of programmed narrative specification

3) Development of programming code to generated programmed narratives

(4) Delivery of FINAL Qced programmed narratives to MW

(5) Addition of other narrative sections based on CIOMS or AESI forms

(6) Narrative review by safety group for non-programmed sections

(7) Include in the study CSR

Automated narrative generation- Overview

- Potentially robust solution for studies with similar design
- Potential to save hundreds of manual hours of narrative writing
- Less chances of manual errors
- Cannot automate sections that need human interpretation

Informed Consent Form

Informed Consent: Definition (ICH-GCP 1.28)

- Voluntary confirmation of willingness of subject to participate in a clinical trial
- Informed about all aspects of trial relevant to the decision to participate
- Should protect the rights of the subject as a clinical study participant

Elements of Informed Consent

Necessary information to be provided to subjects

- That the trial involves research
- Purpose: that the trial is experimental
- Trial treatment and probability of random assignment to treatment
- Trial procedures, alternative procedures/ treatments; everything that will happen to them
- Risks and anticipated benefits
- Subject's responsibilities
- Confidentiality, voluntariness, access to subjects' records

Informed Consent Form (ICF)

- Approved by Ethics Committee
- Language best understood by the subject
- Signed & Dated by the subject
- Signed and dated by person conducting the informed consent process
- Copy to Subject along with the information sheet and a copy at site