



PREPARATION FOR FDA & EMA INSPECTIONS: PRACTICAL INSIGHTS FOR CRO /SITE PERSPECTIVE

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CLINICAL TRIALS SYMPOSIUM
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ARENSIA OVERVIEW

GERMAN COMPANY - HQ IN DUSSELDORF WITH 250 EMPLOYEES (60% MDs)

EIGHT (8) DEDICATED STATE OF-THE-ART EXPLORATORY MEDICINE UNITS WITH PHASE I
INFRASTRUCTURE

SPECIALISTS IN PERFORMING PHASE I / IB/ IIA / PROOF OF CONCEPT PATIENT TRIALS

PROJECT MANAGEMENT | REGULATORY SERVICES HA/EC
STUDY SUPPLY LOGISTICS | QUALITY ASSURANCE

SATELLITE SERVICES VIA PARTNERS: MEDICAL WRITING | DATA MANAGEMENT | BIostatISTICS
CLINICAL LABORATORY BIO-ANALYTICS |IMAGING ETC.

INSPECTION READINESS

! STARTS WITH THE PLANNING PHASE OF A CLINICAL TRIAL !

WELL PLANNED & CONDUCTED CLINICAL TRIAL
ENHANCES THE INSPECTION PREPARATION AT ANY GIVEN
TIME !

AND

PREVENTS FROM NEGATIVE "SURPRISES" ONCE THE
INSPECTION IS ANNOUNCED



REASONS FOR INSPECTION/SITE SELECTION

- FOR CAUSE
- ROUTINE
- TARGETED CLINICAL INVESTIGATIONS INSPECTIONS



COMPLIANCE PROGRAM

BIORESEARCH
MONITORING (BIMO):
CLINICAL INVESTIGATORS

ELECTRONIC SITE SELECTION WIZARD

- KNOWLEDGE OF INVESTIGATOR SITES, SPONSOR OR VENDORS
- FORMER INSPECTION OUTCOME HISTORY OF SPONSORS, VENDORS, INVESTIGATOR SITES
- TRIGGERS: COMPLEX PROCEDURES, SUSPICIOUS DATA
- KNOWLEDGE OF THE CONTINENT, REGION, COUNTRY OR AREA

INSPECTION ANNOUNCEMENT



ROUTINE:

- ANNOUNCED OR UNANNOUNCED
→ FORM 482: NOTICE OF INSPECTION
- RELIES MOSTLY ON DOCUMENTS FROM APPLICATION DOSSIER (DATA LISTINGS, CLINICAL STUDY REPORT)
- POSSIBLE OUTSIDE OF US: DIRECT CONTACT TO PI WITHOUT NOTIFICATION OF SPONSOR



ROUTINE:

- FORMAL ANNOUNCEMENT LETTER
- DETAILED AGENDA
- REQUEST FOR DOCUMENTS



FIRST STEPS

PREPARE A PLAN OF ACTION

- ASSIGN ROLES AND RESPONSIBILITIES
 - GOOD ORGANIZED PERSON TO COORDINATE PREPARATION
- INFORMING SPONSOR, REGULATORY BODIES, LABORATORIES & ANY OTHER INVOLVED VENDORS
- SET-UP REGULAR MEETINGS OF PREPARATION GROUP
- ESTABLISH A MANAGEMENT TOOL (TABLE, PROJECT MANAGEMENT SOFTWARE)
 - MAKE SURE ALL POINTS ARE ADDRESSED IN TIME
- PLAN A MOCK INSPECTION AUDIT, IF THERE IS SUFFICIENT TIME



PLANNING OF RESOURCES

PLANNING OF RESOURCES FOR PREPARATION:

BE PREPARED:

→ EXTRA HOURS AND EXTRA COSTS ARE NEEDED

ONE VERY WELL ORGANIZED PERSON TO COORDINATE PREPARATION,
DEPENDING ON TIMELINES → 1 FTE

ROLE OF INTERNAL QUALITY CONTROL (QC) AND QUALITY ASSURANCE
(QA) IS VERY IMPORTANT → PLAN RESPECTIVE RESOURCES



PREPARATION – DIFFERENT ASPECTS

- SCOPE OF INSPECTION – INSPECTED TRIAL
- ACCESS
- LOGISTICS
- COMMUNICATION
- TRAINING/INFORMATION



PREPARATION – DIFFERENT ASPECTS

SCOPE OF INSPECTION – INSPECTED TRIAL

- TRIAL CONDUCT / DOCUMENTATION – REVIEW
- IMP
- LABORATORY & OTHER ASSESSMENTS → VENDORS
- BE AWARE OF PROBLEMS, IF ANY, RATHER THAN DESPERATELY TRY TO SOLVE EVERY PROBLEM
- KNOW WHERE THE GAPS ARE AND THINK ABOUT ADEQUATE EXPLANATIONS UPFRONT



PREPARATION – DIFFERENT ASPECTS

SCOPE OF INSPECTION – INSPECTED TRIAL

PREPARATION OF CHECKLISTS BASED ON:



COMPLIANCE PROGRAM GUIDANCE
MANUAL FOR FDA STAFF

BIORESEARCH MONITORING (BIMO):
CLINICAL INVESTIGATORS



GUIDELINE FOR GCP INSPECTION
REPORTING:
ANNEX I - PROCEDURE FOR
CONDUCTING GCP INSPECTIONS

REQUESTED BY THE EMA:
INVESTIGATOR SITE

PREPARATION – DIFFERENT ASPECTS

ACCESS

- PAPER-BASED DOCUMENTATION (FDA/EMA)
- FACILITIES
- ARCHIVE
- PHARMACY/ DEPOT (IMP RETENTION SAMPLES - FDA)
- ACCESS TO ELECTRONIC SYSTEMS (EMA)
 - INDIVIDUAL ACCESS CODES AND PASSWORDS
 - READ ONLY ACCESS
 - PRINTING OF DOCUMENTS MUST BE POSSIBLE
 - AUDIT TRAIL MUST BE AVAILABLE
 - SHOULD ALLOW REVIEW IN AN EFFICIENT MANNER, ANALOGOUS TO WHAT IS POSSIBLE WITH PAPER



PREPARATION – DIFFERENT ASPECTS

LOGISTICS

- OFFERING HELP FOR TRANSPORT/HOTEL
- LOCATIONS & EQUIPMENT (BOARDROOM – BACK OFFICE)
- REFRESHMENT/CATERING (CLARIFY RESTRICTIONS/INTOLERANCES)
- INSPECTION DOCUMENTATION: SCRIPT, INSPECTION MASTER FILE
- AVAILABILITY OF PERSONNEL WHO HAVE LEFT THE COMPANY (IN CASE THEIR EXPERTISE IS REQUIRED – E.G. BIOEQUIVALENCE – RETENTION SAMPLING)
- ATTENDANCE OF SPONSOR REPRESENTATIVE AT THE BACK OFFICE, IF REQUESTED





PREPARATION – DIFFERENT ASPECTS



COMMUNICATION

- INSPECTOR'S BACKGROUND
- SUITABLE CONTACT PERSONS (EXPERTISE AND PERSONALITY) FDA:
KEY PERSON (VOLUNTARY, BEST FIT)
- APPROPRIATE TRANSLATOR (INDEPENDENT & WELL TRAINED)
- COMPANY'S NOTABILITIES ONLY PRESENT AT OPENING AND CLOSURE
MEETING

PREPARATION – DIFFERENT ASPECTS

TRAINING/INFORMATION

- TRAIN THE PARTICIPANTS

- PROFESSIONAL APPEARANCE

- HOW TO BUILD AND MAINTAIN A RELATIONSHIP

- DO'S & DON'TS

- QUESTION AND ANSWER TECHNIQUES

- MOCK INSPECTION TRAINING



INFLUENTIAL DIFFERENCES – FDA <-> EMA

		
APPROACH	DATA/SAFETY - NARROW GCP SCOPE	SYSTEM – BROAD GCP SCOPE
INSPECTOR - QUALIFICATION	GENERALIST	CLINICAL TRIAL SPECIALIST
EXPERIENCE WITH TEAMWORK	INSPECTORS MOSTLY WORK ALONE	INSPECTORS OFTEN WORK IN A TEAM (LEAD INSPECTOR – LI, REPORTING INSPECTOR, REPORTING INSPECTORATE –RI)

INFLUENTIAL DIFFERENCES – FDA <-> EMA

		
CLOSE-OUT MEETINGS	WRITTEN FDA 483 FORM AT CLOSE OUT (TO BE COUNTERSIGNED)	FEEDBACK ON SYSTEMATIC ISSUES – DETAILS IN REPORT
„IMMEDIATE“ RESPONSE	CONFIRMATION OF ACCEPTANCE: UPON CLOSE-OUT (VERBALLY) OR IN WRITTEN UNTIL 15 DAYS AFTER INSPECTION	DRAFT REPORT PROVIDED FOR REVIEW
GRADING OF FINDINGS	OAI – OFFICIAL ACTION INDICATED VAI – VOLUNTARY ACTION INDICATED NAI – NO ACTION INDICATED	CRITICAL MAJOR MINOR

INSPECTION STYLES

	
FOCUSED ON DATA REVIEW AND SUBJECT SAFETY DATA	FOCUSED ON VERIFICATION OF SYSTEMS: ➤ ETHICAL SUBJECT RECRUITMENT ➤ RELIABLE DATA
VERIFICATION OF DATA SUBMITTED IN THE NDA (NEW DRUG APPLICATION)	AVAILABILITY OF ESSENTIAL DOCUMENTS
DATA LISTINGS/CSR RESULTS ARE CHECKED AGAINST SOURCE	COMPLETION OF PRE-INSPECTION DOSSIER IS REQUESTED: ORGANIGRAM, QMS DESCRIPTION, SOP LIST, LIST OF TRIALS, STAFF QUALIFICATION, ETC...
TRAINING & QUALIFICATION ONLY IN FOCUS WITHIN CRITICAL ISSUES	VERIFICATION OF A ROBUST QUALITY SYSTEM



THANK YOU!

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