CPI Certification Guide – September 2009

General Information

Benefits of Certification

APPI offers the Certified Physician Investigator (CPI®) examination to qualified physician investigators. Region-specific exams are offered for North America and ICH (rest of the world). Certification as a CPI® signifies that a physician possesses knowledge sufficient for the safe and ethical conduct of a clinical trial in accordance with the appropriate ethical, medical, scientific, legal, and regulatory standards.

The written CPI® examination is a measure of a candidate's general skills and knowledge of the information needed for the CPI® to perform this role effectively. Certification is granted in recognition of the applicant's documented education, training, and experience as a primary, sub- or co-investigator OR monitor, supervisor, or designer of clinical trials and based upon successful completion of the written CPI® examination. By awarding the title of Certified Physician Investigator (CPI®), APPI is formally recognizing the professional physician investigator or pharmaceutical physician who has provided evidence that he or she meets accepted professional standards.

Industry Recognition

Based on a survey of CPIs, those surveyed believed that enhanced professional standing, increased company marketability (for CROs), personal satisfaction, and enhanced recognition by peers and supervisors were the primary anticipated advantages for becoming certified.

About the Exam

Physician Investigator Definition

A physician investigator is a physician (MD or equivalent degree) who serves as the primary, sub- or co-investigator or monitors, supervises, or designs clinical trials and accepts responsibility for the safe and ethical conduct of a clinical trial, herein defined as a systematic experiment designed to evaluate the pharmacokinetics, pharmacodynamics, pharmacoeconomics, safety, efficacy, and effectiveness of a drug, biological, medical device (therapeutic or diagnostic), procedure or other intervention involving human participants.

Physician Investigators perform, at a minimum, the following tasks:

- Responsible for the safe and ethical conduct of a clinical trial
- Evaluates the study proposal and decides on participation
- Facilitates or verifies formal approvals according to regulatory requirements and ICH GCP
- Ensures that all site initiation activities are performed to start and conduct the study
- Participates in the selection of trial subjects according to the recruitment strategy
- Performs and/or supervises the conduct of study-related procedures and monitors the safety of the trial subjects and investigational staff
- Collects accurate and verifiable data and other essential study documents

- Ensures compliance with regulatory requirements and ICH GCP, the protocol and the handling of the investigational product
- Communicates with subjects, sponsor's personnel and IEC/IRB
- Ensures adequate close-out of the study

Requirements for Admission to the CPI® Exam

To be eligible for the certification examination, an applicant must meet specific education, employment, training, and professional competency requirements.

Education: The applicant must hold a medical physician degree (M.D. or equivalent degree) and have a current medical license to practice in the state/region where employed and be in good standing with all state/province/locality licensing and regulatory authorities and certifying bodies.

Employment: Complete all sections of the application that pertain to employment. Employment is broadly defined to include paid services, fellowships, internships, and volunteerism. Employment experience must include service as a primary, sub-, or co-investigator in one or more clinical trials for the last two (2) years, **OR** a medical monitor, supervisor, or designer of one or more clinical trials for the last two (2) years, **OR** the successful completion of an accredited clinical research degree or clinical fellowship program of at least one (1) year's duration.

Licenses and Registrations: A current medical license to practice medicine in the state/province/locality is required of all CPI® exam candidates. Complete all sections of the application that pertain to state/regional licenses and registrations. The applicant is responsible for including copies of all current state licenses and registrations held by the applicant. Failure to include this documentation may delay the processing of the application.

Investigator Agreements, IRB Approval Letters or Protocol Approval Signature Pages: The applicant is responsible for including documentation signed in each of the last two years (e.g., Form 1572 or IRB approval letter) that demonstrates involvement in clinical research after the last two years. This evidence can be 15720 or other investigator agreements, IRB approval letters or protocol approval signature pages. Failure to include this documentation may delay the processing of the application, or may result in ineligible status.

CV: **A (no less than one-year-old) signed and dated CV is required and must be included with the application.** By signing and dating the CV, the applicant affirms that the information contained in the CV is truthful and current. Failure to include this documentation may delay the processing of the application, or may result in ineligible status.

Additional Application Information

Personal Information: Complete all sections of the application that pertain to personal information. This information is needed in order to facilitate communication with the applicant. Applicants should include maiden names if they are needed to confirm education, work experience, or training requirements. Provide complete information including all zip/postal codes, telephone numbers,

and e-mail addresses in order to expedite processing. During the application and certification process, it is the applicant's responsibility to keep APPI informed of current addresses so that he or she will continue to receive all certification updates, exam scores, training information, and renewal notices.

Original Signature and Verification of Information: An original signature must be on the application. Applicants are expected to provide truthful and complete information. Any application missing information or found to be dishonest will not be considered for the certification program. Should falsification of the application be discovered after the exam has been taken, passed and certification awarded, the certification will be revoked.

Application Process Overview

To be eligible for the CPI® examination, a candidate must submit a completed application along with collateral materials including CV, copies of current medical licenses and registrations, and documents verifying experience. The application steps include:

1. Review the CPI® Certification Guide and the Exam Operations Manual prior to completing the application. Follow the instructions given, and address any questions to APPI. Failure to follow the instructions can lead to the denial of an application.

2. Review the competency requirements. To take the CPI® examination, an applicant must meet certain educational, employment, training, and professional competency requirements. **All accrued education, work experience, and training must be completed prior to the exam date. DO NOT submit an application before you have acquired all the work experience, education, and training needed for eligibility.**

3. Complete and mail the application. The completed application must include: 1) a current signed and dated CV, 2) a copy of all current state medical license(s)/registration(s), and 3) three copies of signed regulatory forms, such as the 1572, IRB approval letters, or protocol approval letters that cover the last two years that demonstrates your involvement in clinical research.

4. Mail the application and application fee. A completed application and fee must be received at APPI by July 13 before processing begins. We will accept applications until July 27 with a $150 late fee.

5. Allow sufficient time for application review. Applicants are encouraged to submit their applications and collateral materials as early as possible to allow for any unanticipated delays. APPI may confirm an applicant's employment and work experience and will process the application as quickly as possible. Major delays are often caused by incomplete applications or by missing collateral information.

6. Taking the examination. If an applicant is approved to take the CPI® examination, they will be informed via email that they are now eligible to take the examination.

7. Wait for the examination results. In order for statistical analyses to be completed on the CPI® examination, examination results will be mailed approximately six weeks after the examination date.

Examination results will be released in writing via mail only. Examination results will not be given via telephone or fax.

Language

The CPI® Certification Exam is provided in the English language.

Please note: Exam candidates may bring an English-German / Spanish / Dutch / Italian / etc. dictionary to the exam. The dictionary will be inspected by the proctor prior to and after the exam is completed. Any attempt to compromise the exam will be grounds for immediate dismissal from the site, invalidation of the exam score, and possible legal action.

CPI® Exam Content

Four major performance areas account for the examination content. The major content areas and the associated job tasks, as well as the number of exam questions in each area are listed below:

I. Study Management (12 questions)

A. Protocol Evaluation

1. Understand the trial design including its scientific, statistical and ethical integrity, as it applies to their situation
2. Comply with regulations and guidances regarding drugs, medical devices, and biologics
3. Assess protocol for clarity, thoroughness, logistical, operational and therapeutical feasibility, maintaining subject safety and welfare, inconsistencies, etc.
4. Determine subject population availability
5. Assure availability of qualified research staff and required equipment, facilities, and infrastructure
6. Develop timelines for conducting and completing the clinical trial
7. Address concerns and questions with the Sponsor/CRO (e.g., patient population, Sponsor/CRO expectations, enrollment, study procedures)
8. Negotiate alternatives to improve protocol implementation (e.g., inclusion/exclusion criteria, concomitant medications, protocol timelines, logistics)
9. Ascertain the safety and expected therapeutic effects of the investigational product by verifying the preclinical and clinical research done so far (using the investigator brochure)

B. Site Preparation and Initiation

1. Select the investigational staff and assign roles and responsibilities
2. Assure appropriate training of the investigational staff and attend and participate in the study initiation meeting (e.g., Investigator meeting), if applicable
3. Ensure that a recruitment strategy and study management plan is developed to direct the successful conduct of the trial
4. Assure the availability of validated operational and administrative tools and processes (e.g., hardware and software, recording devices)
5. Ensure consistency between the sites' standard operation procedures (SOPs) and the study requirements

6. Check on congruence of data collection tools (e.g., case report form [CRF], electronic data capture [EDC]) with the study protocol
7. Collect and submit all essential pre-study documents required by ICH GCP and/or local regulatory requirements
8. Schedule and coordinate pre-study site visit with Sponsor/CRO's representative
9. Complete region/country specific regulatory documents for Sponsor/CRO.
10. Prepare space for study-related equipment and supplies (i.e., storage of study investigational products, laboratory supplies, CRFs/eCRFs)
11. Prepare and submit required IRB/IEC documents (e.g., informed consent, advertisements, protocol)
12. Integrate proposed clinical trials with current research Activity

II. Project Activities (50 questions)

A. Investigational Product Accountability

1. Receive investigational product from Sponsor/CRO and inventory supplies
2. Ensure investigational product supplies are kept in a secure location according to the required storage conditions
3. Dispense investigational product (e.g., calculate dosage) according to the protocol
4. Retrieve used/unused investigational product from subject and assess compliance
5. Verify the expiry date and arrange proper relabeling activities where needed
6. Monitor the investigational product stock and order supplemental supplies, if needed
7. Maintain randomization and emergency codes of investigational product dispensing
8. Keep an accountability log for each trial subject, documenting investigational product dispensed, returned and disposed
9. Manage controlled substances, if applicable
10. Prepare emergency use report, if applicable

B. Laboratory and Diagnostic Issues

1. Ensure proper collection, processing, and shipment of specimens (e.g., centrifuge, preparation of slides, freezing, refrigeration)
2. Handle samples according to required standards
3. Ensure maintenance of equipment and documentation thereof (e.g., calibration reports, maintenance logs)
4. Interpret laboratory values and alerts according to protocol and subject safety
5. Assure current certification/licensure and normal ranges

C. Adverse Events

1. Determine causality of expected or unexpected results associated with investigational products
2. Document, classify, and manage adverse events
3. Assure proper medical care and follow-up until resolution or stabilization of adverse events

D. Closeout

1. Ensure timely completion of data collection tools

2. Assure a completed investigational product accountability, and organize the receipt and return/disposition of the investigational product and other supplies
3. Assure close-out reporting to the sponsor, IRB/IEC and/or other parties involved
4. Ensure filing, archiving, and retrieval of the essential Documents
5. Assure follow-up medical care for study subjects, as Applicable
6. Assure financial reconciliation against the (trial) agreement contract, including timely and accurate compensation to the staff and/or study subjects
7. Determine disposition of study-related materials per Sponsor/CRO requirements
8. Prepare for and respond to Sponsor/CRO, regulatory, or internal audits

E. Responsibilities and Obligations

1. Conduct research in accordance with the clinical trial agreement specific to the region/country
2. Facilitate or verify formal approvals according to ICH GCP and any regional or local requirements, if applicable.
3. Ensure that all required documents are submitted for approval to the IRB/IEC
4. Check whether the IRB/IEC approval letter is adequate and details of the IRB/IEC composition are on file
5. Assure that the IRB/IEC is in compliance with regulations and ICH guidelines
6. Provide progress reports to IRB/IEC annually, or as requested, and obtain re-approval
7. Ensure compliance with regional requirements (FDA, ICHGCP, European Union Clinical Trial Directive) as applicable.
8. Implement and document corrective actions
9. Maintain the continuity of the clinical trial while satisfying obligations to the Sponsor/CRO and/or monitor
10. Ensure site is prepared for any Regulatory/Sponsor/CRO audits (e.g., consequences, requirements, deficiencies)
11. Maintain current knowledge of clinical research issues (e.g., ICH/GCP guidelines)
12. Follow HIPAA regulations
13. Maintain communication with IRB/IEC regarding
    - continuing review
    - serious adverse events
    - IND safety reports
    - protocol amendments
    - protocol deviations/violations
    - informed consent modifications
    - changes to investigator agreements
    - final report

III. Subject Management (50 questions)

A. Recruitment

1. Participate in the selection of trial subjects according to the recruitment strategy
2. Ensure compliance with data protection legislation
3. Maintain subject screening/enrollment log

B. Informed Consent

1. Ensure the protection of human subjects (e.g., Declaration of Helsinki; ICH GCP and other regional standards, as applicable)
2. Explain study to subject (e.g., purpose, duration, risks/benefits)
3. Assess subject understanding of study requirements
4. Obtain all required signatures (e.g., legal guardian, assent of youth, physician) to document informed consent
5. Provide subject a copy of informed consent form
6. Document obtaining informed consent in source document
7. Obtain informed consent from vulnerable subject populations

C. Scheduling/Screening

1. Screen potential subjects to obtain medical history (medications/medical/surgical history)
2. Verify the eligibility of potential trial subjects to ensure that all entered subjects meet the inclusion/exclusion criteria
3. Schedule subjects
    a. determine length and timing of visits
    b. coordinate subject visits with support services (e.g., subject, physician, ancillary staff, coordinator)
    c. determine pay or responsibility for designated study visit

D. Study Conduct

1. Perform and/or supervise the conduct of study-related procedures and monitor the safety of the trial subjects and investigational staff
2. Manage and motivate the investigational staff and other disciplines involved, and take measures to minimize any potential risks
3. Establish and maintain professional relationship with trial subjects
4. Administer the investigational product following the randomization schedule and maintain the blind as applicable
5. Ensure that study related procedures and measurements are performed at the required time points, according to the study management plan
6. Enable monitoring activities, provide monitoring space and meet with the sponsor's monitor
7. Follow-up or take corrective actions when requested by the sponsor's monitor
8. Inform the sponsor and IRB/IEC of any changes to the protocol or safety concerns and submits progress reports to the IRB/IEC, in full compliance with ICH-GCP and any other regional requirements.
9. Prepare the study site for audits & inspections
10. Respond to or facilitate response to audit/inspection findings
11. Facilitate effective communications with sponsor, IRB/IEC, institution and regulatory authorities, if applicable

IV. Documentation and Administration (13 questions)

A. Case Report Forms

1. Review inclusion/exclusion criteria
    a. make required calculations (e.g., convert units of measurements)
    b. determine concomitant medications, therapies, and adverse events
    c. review medical history

2. Collect accurate and verifiable data and other essential study documents
3. Record the data in the CRF or other data collection tools (e.g., EDC)
4. Transmit data (e.g., fax, express mail) as required by Sponsor/CRO

B. Source Documentation

1. Confirm source documents to be used for the study
2. Confirm data which will be directly entered onto the Case Report Form
3. Collect the trial data and complete the appropriate source Documents
4. Assure access to source data by authorized parties, in accordance with ICHGCP, and protect confidentiality by limiting unauthorized access
5. Collect and file all other essential study documents as required per ICHGCP and or local regulatory requirements
6. Assure query resolution with the sponsor
7. Incorporate applicable historical documents (e.g., surgical reports, pathology reports, medical history)
8. Obtain and record ancillary services reports (e.g., x-ray, pathology, ECG, laboratory)
9. Maintain progress notes
10. Document written, electronic, and verbal communication with study contacts (e.g., subject, Sponsor/CRO, IRB/IEC, laboratory)
11. Prepare for monitoring visits
12. Document protocol deviations/violations

C. Financial/Budgetary Issues

1. Determine the site budgetary requirements
    a. determine anticipated study-related costs and profit margin (e.g., fixed fees, overhead, direct and indirect costs)
    b. negotiate fees for associated services (e.g., laboratory, radiology, study-specific services, advertising)

2. Negotiate budget and payment schedule with Sponsor/CRO
3. Review letter of agreement (contract) for completeness
4. Review sponsor indemnification
5. Reconcile outstanding financial considerations for physician payments and ancillary services (e.g., advertising, support services) sponsor/CRO payments to site subject reimbursement
6. Finalize the trial/financial agreement with the sponsor

125 Total Questions

CPI® Exam Preparation

To prepare for the **North American CPI® Exam**, candidates should review and be familiar with the following documents:

21 CFR Parts 11, 50, 54, 56, 312, 812, 814
45 CFR Part 46, 160, 164 (HIPAA Privacy & Security)
Investigator information sheets
FDA information sheets
FDA forms 1572, 483, 3500A
ICH GCP Guidelines (e.g. E2—Clinical Safety, E6—GCP, E8 General Considerations for Clinical Trials)
Declarations of Helsinki
Belmont Report
Informed Consent, (CenterWatch publication)

Other useful websites include:

A current copy of the regulations and other regulatory materials may be found at http://www.fda.gov or http://www.regsource.com.
http://www.fda.gov/cdrh
http://www.fda.gov/cdrh/devadvice
Agency for Healthcare Research and Quality http://www.ahcpr.gov/
Department of Health and Human Services http://www.os.dhhs.gov/
AMA Code of Medical Ethics: American Medical Association

To prepare for the **ICH CPI® Exam**, candidates should review and be familiar with the following documents:

ICH GCP Guidelines (e.g. E2—Clinical Safety, E6—GCP, E8 General Considerations for Clinical Trials)
Declarations of Helsinki
EN-540 (medical devices)

Reference book(s) (suggested, not required) on:

Drug development
Study design and biometric principles, e.g., blinding, control groups, randomization, etc.
Pharmacokinetic and pharmacodynamic principles of drugs
A Guide to Clinical Drug Research: 2nd Edition, A. Cohen & J. Posner (2000). ICBN 0-7923-6172-5

Practice Test: APPI offers an optional online Investigator practice exam to help candidates prepare for the CPI® examination at http://www.acrpnet.org/MainMenuCategory/Certification/ExamPreparation/FDAOnlinePracticeExam.aspx.

Practice exams allow candidates to prepare for the CPI® examination by familiarizing themselves with the examination format and question types. When a practice exam has been

completed, the system immediately provides a candidate with results by displaying diagnostic feedback. This feedback may assist candidates by reducing testing stress levels and enable candidates to make effective use of their study times.
Online practice tests allow access any time, any where, through any computer with Internet access. The cost of the online practice exam is $75. Payments for the practice exam are made directly to ACRP.

Sample Questions: The following four questions were taken from the CPI® examination question item bank and serve as samples of the question type and question content found on the CPI® examination.

1. 1B 2 (Application)
All of the following are likely stratification factors in a randomization schedule EXCEPT

A. glucose level.

B. caloric intake.

C. disease severity.

D. prior study participation.

Answer: D Stratification is based on a factor that could potentially impact the outcome of the study and is performed to assure adequate numbers of subjects in each of the strata. The best answer is D. Glucose level, caloric intake, and disease severity all are common stratification practices. Although subjects may continue to another stage of a study based on prior participation, for example, after completing a double-blind portion of the study all subjects receive open-label drug, this would be considered a study continuation or sub-study.

2. 3A 67 (Analysis) In a Phase I oncology study, the MOST appropriate time to approach a patient about joining an experimental drug study as a research subject participant is when

A. their illness is becoming worse and they are not responding to conventional therapy.
B. they are feeling well and not experiencing a lot of stress.
C. they lose their health insurance plan and have to pay more than the co-pay for their visit.
D. they have been laid off from their job, and they have more time on their hands and less money.

Answer: A Because of the potency of antineoplasitic drugs, Phase 1 oncology studies are usually conducted in patients who have no other therapeutic alternatives. Patients volunteer to participate so that the basic pharmacokinetic information can be obtained. Although subjects may enroll when they are feeling well, the risk involved with these types of drugs may outweigh the benefits. Enrolling a subject because they have lost health insurance or their job may be considered coercive for the patient.

3. 3C 218 (Physician Only –Application) A protocol for a new drug used to treat cystic fibrosis (CF) excludes patients who have received antibiotics or corticosteroids within 2 weeks of screening, as well as patients who have started a new chronic medication for CF within 2 weeks of screening. Which of

the following patients would be INELIGIBLE to participate in this study?

A. A patient who was diagnosed 2 weeks ago with allergic rhinitis for which a nasal antihistamine was prescribed to be taken on a p.r.n. basis.
B. A patient who is on longstanding treatment with prednisone to maintain pulmonary functions.
C. A patient who was admitted to the hospital one month ago and was put on IV antibiotics for a pulmonary infection and discharged after 3 days with a 1-week course of oral antibiotics.
D. A patient who was seen in the emergency department 10 days ago for symptoms presenting as a migraine headache. The patient was treated with an injection of Demerol and discharged.

Answer: B B is the only response where a corticosteroid (prednisone) is given and it is given to treat pulmonary function, which is a treatment for CF. Patient A has none of the exclusion criteria stated in the question. Patient C has met the 2 week time period since receiving antibiotics. Patient D was treated for a migraine headache, not CF, and Demoral is not a corticosteriod.

SCENARIO 9109.00 1

SCENARIO

The following question refers to this Scenario.

A research site is currently enrolling two studies for osteoarthritis (OA) of the knee. Entry criteria are listed in the table below.

Study A	Study B
>/= 40 years of age	>/= 45 years of age
OA of the knee for > 1 year	OA of any site for > 6 months
taking daily anti-inflammatory	reports daily pain due to OA
cannot be taking aspirin for any reason	may use </=325 mg of aspirin QD
cannot take any antacids	during the study

4. 3C 243 (Physician Only – Application) A subject is in the office for a screening visit for Study A. Although he has osteoarthritis of the knee, he states he takes a daily anti-inflammatory for the OA pain in his hands. He reports he takes acetaminophen for occasional headaches. Which of the following is the investigator's BEST course of action?

A. Call the sponsor for an exception of daily anti-inflammatory use for OA other than knee.
B. Request the subject use only acetaminophen for pain relief during the study.
C. Decline the subject entry into Study A, but enroll into Study B.
D. Inform the subject he does not qualify for Study A or B.

Answer: C
Although the subject is not eligible for the study he was initially screened, he appears to be eligible for Study B. Upon signing that Informed Consent Form, the subject can be screened for Study B. The sponsor should not permit this type of exception to the study. Option B does not make the subject eligible by discontinuing the anti-inflammatory drug.

Option D is incorrect because the subject may qualify for Study B.

Letter and Certificate: Candidates who pass the examination will receive a letter confirming their new certification status and a certificate suitable for framing with an expiration date. The letter can be photocopied and distributed to sponsors as needed.

Examination Retakes: Candidates who fail the examination must reapply to take the CPI® examination. The reapplication process includes submitting a current application and requested collateral materials as well as paying any current examination fees. There is no waiting period and no limit to the number of times a candidate can retake the examination.

Contact Information

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Non-Discrimination Policy

APPI does not discriminate on the basis of age, gender, race, disability, marital status, sexual preference, religion or national origin.