

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER) GUIDE FOR PARTICIPATION IN THE FOOD AND DRUG ADMINISTRATION (FDA)/NATIONAL CANCER INSTITUTE (NCI) INTERAGENCY ONCOLOGY TASK FORCE (IOTF) FELLOWSHIP TRAINING PROGRAMS

I. PURPOSE

The purpose of this guidance document is to formalize Center policy concerning participation in the FDA/NCI IOTF Fellowship Training Programs, and establish the procedures under which the Fellow will engage in mentored scientific studies and review practices in a CBER research laboratory or another CBER facility.

The program's purpose is to educate scientists and clinicians about medical product research and review practices and regulations in hopes that an increased understanding of the FDA review process will enable scientists to more efficiently develop and bring to market important new products for the prevention, diagnosis and treatment of cancer.

II. REFERENCES

Joint Fellowship Training Program, <http://iotftraining.nci.nih.gov>

Overview of IOTF Program, <http://iotftraining.nci.nih.gov/IOTFJointProram.ppt>

Economy Act, 31 U.S.C. § 1535, and 42 U.S.C. § 285a-2(b)(3) Section 301 of the PHS Act (42 U.S.C. 241), and Section 742 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 3791(b).

III. HISTORY

Version 1 – First issuance of this SOPP.

Definitions

- For the purpose of this document: **Non-FTE persons** will define individuals in non-civil service appointments, but who are:
 - Engaged in scientific studies and investigations using FDA/CBER facilities; and/or
 - Involved in temporary exchange agreements between FDA and another federal agency.
- **FTE** – Full-Time Equivalent or Full-Time Employee
- **Conflict of Interest:** an activity or relationship with another person or organization that does or could impair the Fellow's objectivity in performing the mentored review training or that could give, or appear to give, an outside person

and unfair competitive advantage. Information that is relevant to a conflict of interest determination includes, but is not limited to, stock holdings and investments of the Fellow, the Fellow's spouse and minor children; current positions held or under negotiation; any contracts, grants or Cooperative Research Development Assignment (CRADA) on which the Fellow is working or has under negotiation; any other sources of income, and any other relevant information that may have a bearing on the Fellow's proposed participation in the mentored review training portion of this program.

IV. BACKGROUND

In February of 2005, FDA entered into a joint training program with NCI, via two Interagency Agreements as a part of the Interagency Oncology Task Force (IOTF) Initiative, to train a selected cadre of M.D., M.D. - Ph.D. and Ph.D. scientists in Critical Path research (i.e., research in support of product review) and regulation.

A fundamental part of the mission of NCI is to develop and to facilitate the development and use of drugs/biologics, regimens, and devices effective in treating, preventing, or ameliorating morbidity and mortality associated with cancer. A primary aspect of the FDA mission is to conduct regulatory review to assure that medical products demonstrate the appropriate balance of safety and efficacy for particular disease treatment, mitigation, or prevention indications before they are approved for those indications.

Fellows will be trained in preclinical oncology research, cancer prevention, clinical trials methodology, medical product, and other regulatory research and review. By combining training in cancer-related scientific research and research-related regulatory review, this program will help fellows learn to bridge the development and review processes. If heightened awareness of the requirements of regulatory review of safety and efficacy can be incorporated into the plan of development and testing from the early stages, NCI and FDA will be better equipped to achieve a common goal: bringing safe and effective drugs, regimens, and devices from the bench to the bedside in a more rapid and effective manner.

The IOTF Initiative is composed of two Fellowship Training Programs and four pathways to provide training:

- A. Medical Fellowship Training:** 1) Clinical Oncology Product Research/Review for Oncology Fellows; and 2) Clinical Oncology Product Research/Review for Board Certified (BC) Oncologists
- B. Postdoctoral Fellowship Training:** 3) Oncology Product Research/Review Fellows; and 4) Cancer Prevention Fellows.

V. POLICY

Types of Appointments:

While at FDA, all Fellows are mentored by a senior member of the FDA scientific staff in regulatory processes and are expected to participate in research projects related to medical product development. Fellows selected for appointment to programs 1 & 2 (fellows involved in

clinical studies or patient care) will be hired by NCI as **FTEs** and will come to the FDA for a portion of their fellowship on an official detail. Fellows selected for appointment to programs 3 & 4 (fellows who do not participate in clinical work) will be hired as contractors (**non-FTEs**) through the NCI Cancer Research Training Award (CRTA) Program, and will spend a significant portion of their time at FDA. The four fellowship opportunities are briefly described below:

1. **Clinical Oncology Product Research/Review for Oncology Fellows:** This fellowship trains individuals in aspects of clinical trials methodology and analysis, epidemiology, clinical aspects of medical product development, and regulation as it relates to the clinical research and development process to facilitate the movement of drugs, biologics, and devices from the basic bench science to commercialization. Fellows in this program spend the first year at NCI and train in the participating oncology-training program followed by a maximum of two years training at FDA. While at FDA, fellows receive formal training and mentoring in the relevant federal statutes, regulations, principals and practices of FDA medical product review, including issues related to clinical trial design, clinical pharmacology, monitoring of clinical trials, identification of biomarkers, and pharmacoepidemiology. The program timeframe will be for up to three years and include up to two fellows per year.
2. **Clinical Oncology Product Research/Review for Board Certified (BC) Oncologists:** This fellowship trains physicians who have already completed their clinical oncology training. As part of this program, participants are trained in aspects of the drug, biologic, or device development and related issues and standards for assessing medical product safety and efficacy, to facilitate the movement of drugs, biologics, and devices from basic bench science to commercialization. While at FDA, fellows receive formal training and mentoring in relevant federal statutes, regulations, principals and practices of FDA medical review, including issues related to the assessment of safety and efficacy, for limited human exposure in clinical trials, and later potential exposure to the broader patient population post-marketing approval. This is a one year program for up to three fellows per year.
3. **Oncology Product Research/Review Fellows:** This fellowship trains individuals in the aspects of research and review of the medical product development process to facilitate the movement of drugs, biologics, and devices from the bench to the bedside. Fellows may spend up to a maximum of two years at FDA. While at FDA, fellows receive formal training and mentoring in the relevant federal statutes, regulations, principals, and practices of FDA medical product review, including issues related to product development (e.g., manufacturing processes, production, purification, characterization, testing, pharmacoepidemiology, manufacturing, post-marketing surveillance, and mechanisms of action/pathogenesis of disease). The program timeframe is for up to two years and allows for up to six fellows per year.
4. **Cancer Prevention Fellows:** This fellowship provides research training within the Cancer Prevention Fellowship Program. The NCI and FDA jointly sponsor this fellowship program to provide training in cancer prevention (e.g., chemoprevention, vaccination, and early detection). Individuals are trained in the drug, biologic, or device development and approval processes and their application to study populations (including healthy subjects) to facilitate the movement of novel approaches from the

bench to the community. Combining training in public health, cancer prevention research, and research-related regulatory overview will allow individuals to develop expertise across three disciplines, offering the possibility of designing and implementing cancer prevention clinical trials. In their first year, fellows must pursue a master's degree in Clinical Investigation (M.S.) or Public Health (M.P.H.). For the remaining up to three years, fellows may choose to spend one year at NCI and two years at FDA. While at NCI, fellows learn the principles and practices of cancer and molecular prevention and are expected to develop professional skills, to include grant writing. While at FDA, fellows receive formal training and mentoring in the relevant federal statutes, regulations, principals, and practices of FDA medical product review, including issues related to product development (e.g., manufacturing processes, production, purification, characterization, testing, quality control and assurance, understanding the biology, chemistry, pharmacoepidemiology, manufacturing, post-marketing surveillance, and mechanisms of action/pathogenesis of disease processes). The program timeframe is up to four years and allows for up to two fellows per year.

Eligibility:

- Must be a U.S. citizen or U.S. permanent resident.
- Clinical Oncology Product Research/Review for Oncology Fellows must possess a M.D. or M.D./Ph.D. degree in a relevant field of clinical training.
- Clinical Oncology Product Research/Review for Board Certified (BC) Oncologists trains physicians who have already completed their clinical oncology training (Board certified oncologist).
- Oncology Product Research/Review Fellows must possess a Ph.D., M.D., or M.D./Ph.D. degree and have a minimum of three years of postdoctoral training in a cancer-related topic.
- Cancer Prevention Fellows must possess a Ph.D., M.D. or equivalent degree.

Program Operations:

- The NCI and FDA will each undertake recruitment and advertisement of these programs through various mechanisms including, but not limited to, print ads, web-based advertising, links on the NCI and FDA home pages, through email listservs, and at national meetings.
- The NCI will receive the applications from prospective candidates through the Center for Cancer Research (CCR) Office of Training and Education. An online application will be established and linked from the appropriate NCI and FDA web pages.
- The NCI and FDA will establish a joint Review Committee to screen applications for completeness, eligibility, and aptitude and to select qualified candidates. The Committee will also evaluate the Program's effectiveness and report on the Program's success and the fellow's outcomes.

- The NCI and FDA will develop a web-based system through which approved mentors post summaries of their projects so that Fellows can select among them. The Review Committee will be responsible for final decisions matching mentors to fellows.
- All Fellows will be matched with mentors, who will be responsible for developing and implementing a training plan. Training plans will be reviewed by the NCI/FDA Joint Review Committee and will be updated yearly at the time of renewal.

Mentored Regulatory Review Training

FDA believes that in order for this program to achieve maximum benefits, all IOTF fellows **must** be given access to confidential commercial information and other non-public information, as part of the mentored review training program. Applicants to the IOTF program must disclose any financial interests in any aspects of FDA regulated product development, manufacturing or distribution industry and may not release, publish or disclose non public-information, specifically any of the facts involved or obtained while serving under this program, including confidential commercial information and trade secret matters [see **Section VIII** for specific responsibilities]. **All IOTF fellows' confidential information will undergo review by FDA's IOTF Fellowship Program Manager on a yearly basis.**

To qualify to participate in CBER's mentored regulatory review training, all IOTF Fellows are required to:

- Attend New Employee Orientation
 - Introduction to the FDA, "FDA 101"
- Undergo Personnel Security Clearance
 - Form 85P, Questionnaire for Public Trust Positions
 - Fingerprinting – through the National Cancer Institute
 - FDA Badging
- Be entered into the FDA EASE database, GovTrip System and UFMS
- Obtain appropriate training certifications for new Fellows and yearly re-certification
 - Computer security – yearly on-line training tracked by the Office of the Chief Information Officer (OCIO) Intranet
 - Economic espionage – yearly on-line training tracked by the Office of Communication, Training and Manufacturing Assistance
 - Ethics training (yearly on-line training notification sent by the Office of Ethics and Integrity)

In addition, FTE Fellows are required to follow all standard FTE processes and complete and submit:

- Confidential Financial Disclosure Report: Form OGE 450;
- Regulation Certification for New Employees: Form FDA 2096;
- Certification for Separating Employees (post-employment regulations): Form FDA 2097;

- Request for Approval of Outside Activities: Form HHS 520, as applicable. Those with affiliations to non-FDA institutions will complete an Outside Activities form indicating this association;
- Certification for IOTF Training - Conflict of Interest
- FDA Confidentiality Agreement for IOTF Fellows (Appendix A)

In addition to requirements for all IOTF Fellows, Non-FTE Fellows are required to complete and submit:

- Confidential Financial Disclosure form
- Certification for IOTF Training – Conflict of Interest
- FDA Confidentiality Agreement for IOTF Fellows
 - The acquiring Office will be responsible for ensuring that Fellows mentored in the regulatory review training program are recused from reviewing any materials relating to the interest that presents a “conflict of interest” as defined under “definitions”. Access to non-public information will be denied and the fellow will be recused from mentored review if the Fellow reports a financial interest that presents a conflict of interest. Non-FTE Fellows performing mentored review training will not be required to divest of prohibited holdings.

Funding:

Funding for Fellows is provided by the NCI. NCI pays the fellow’s stipends directly. FDA will provide for Fellows from their own resources and the NCI will reimburse the FDA for actual costs at the end of the second, third, and fourth quarter of each fiscal year (i.e., end of March, June, and September). The following categories of reimbursement are allowed:

1. Supplies and Services: \$22,500
2. Training: \$4,000
3. Travel: \$3,500
4. Mentor Salary: Reimbursement will be provided for salary costs associated with mentoring the IOTF fellows as 20% of the Mentor’s salary up to \$39,080. The funds will be distributed as follows:
 - 1/3 provided to the regulatory Division of the Office hosting the Fellow for administrative salary support;
 - 1/3 provided to the Division hosting the Fellow for administrative support; and
 - 1/3 provided to the Mentor for research laboratory support, which should be spent on costs associated with the Fellow (e.g., contract research Fellow support, equipment maintenance, etc.).

Stipend:

Each stipend will be determined by the individual’s formal education and years of relevant postdoctoral experience. Ph.D.s will receive between \$37,900 and \$53,000. M.D.s will receive between \$42,800 and \$53,000; M.D.s engaged in approved patient contact during the research years at NCI can receive up to \$73,430. Annual increases may be given. Stipends are subject to

change, depending on federal guidelines. Stipend amounts are determined by NCI and paid directly by NCI to the Fellow.

Health Insurance:

Fellows will receive paid individual or family health insurance through the Foundation for Advanced Education in the Sciences (FAES). For more information on FAES, link to <http://www.faes.org/>

Travel and Training:

The mentor in consultation with the Fellow will determine how to appropriately use the allotted amount of “travel” funds. Training is specifically for regulatory training courses organized through the Office of Communication, Training, and Manufacturing Assistance (OCTMA). OCTMA will handle accounting for all IOTF Fellow training courses. The following reviewer training courses should be taken over the two year appointment:

Highly Recommended Courses:

- Reviewer Training
- Biologics law course
- Clinical Trials
- Device Reviewer Training
- Food and Drug Law Course
- Medical Statistics
- Technical Writing for Reviewers

Optional Courses:

- Basic Grammar
- Conflict Management for Reviewers
- Developing Quality Presentations
- Negotiations for Reviewers
- Risk Assessment
- Risk Management
- Risk Communication
- Writing Refresher
- Team Biologics Courses – ORA course

VI. Scope

The policies, responsibilities, procedures, and criteria found in this Guide will be applied to all IOTF Fellows in CBER, as well as all CBER staff.

VII. Forms Used (Forms available through the FDA IOTF Fellowship Program Manager)

- IOTF Program: Online Fellowship Application: <http://cancer.gov/prevention/pob>; visit NCI-FDA Research and Regulatory Review Fellowships Guidelines for Application at <http://iotftraining.nci.nih.gov/IOTFguidelines.pdf>
- Form OGE 450 - Confidential Financial Disclosure Report – **FTE fellow only**
- Confidential Financial Disclosure form – **Non-FTE fellows only**
- FDA Confidentiality Agreement for IOTF Fellows
- Certification for IOTF Training – Conflict of Interest
- FDA 2096 Form – Regulation Certification for New Employees (**FTE fellows only**)*
- FDA 2097 Form – Certification for Separating Employees* (**FTE fellows only**)
- FDA 3398 Form – Commitment to Protect Non-Public Information* (**FTE fellows only**)
- FDA 3391 Form – FDA Security Card Access Request*
- I-9 Form – Employment Eligibility Verification
- Fair Credit Reporting Act of 1970, as amended
- HHS 520 Form – Request for Approval of Outside Activities, as appropriate (**FTE Fellow only**). **For form and more guidance on Outside Activity policies:** <http://intranet.fda.gov/CBER/sopp/7202.htm>
- CBER Personnel Information Checklist (for internal CBER use only)
- DCC-101 Form – Notification of Personnel Change or Correction for CBER Document Control Center and CBER Staff Directory. For form and more information: <http://intranet.fda.gov/CBER/admin/forms.htm>

*For FDA forms use the following link and click on Numerical Listing:

http://intranet.fda.gov/omp/forms/all_forms.htm;

For Non-FTE Fellows, appropriate comparable forms available through the FDA IOTF Fellowship Program Manager

VIII. Responsibility/Routing

Fellow:

- Before reporting to CBER:
 - Complete online application (Online application and catalog available at <http://cancer.gov/prevention/pob>.) For more information link to “application guidelines”: <http://iotftraining.nci.nih.gov/IOTFguidelines.pdf>
 - Applications received by NCI through the Center for Cancer Research (CCR) Office of Training and Education
 - Be fingerprinted, receive NIH badge, and submit 85P background evaluation through NCI/NIH (information regarding clearance of initial background checks will be forwarded to FDA Personnel Security Office)
 - Once application is accepted and mentor is identified
 - FTE fellows – Employment offers are made through DHHS personnel and Interagency Detail mechanism to work at FDA
 - Non-FTE fellows – Hired through the NCI CRTA process
 - All Fellows attend New Employee Orientation (Introduction to the FDA “FDA 101”)

- Adhere to all established policies and procedures set forth by CBER for the IOTF Fellowship Training Programs

- Complete the following documents:
 - Personnel Information Checklist
 - SF-85P (Questionnaire for Public Trust Positions);
 - FDA 3398 Form (or comparable form for non-FTEs) – Commitment to Protect Non-Public Information
 - FDA 3391 Form - FDA Security Card Access Request
 - I-9 Form - Employment Eligibility Verification
 - Fair Credit Reporting Act of 1970, as amended
 - DCC-101 Form – Notification of Personnel Change or Correction for CBER Document Control Center and CBER Staff Directory
 - EASE FDA Employee Security Statement

- Return Personnel Information Checklist, FDA 3398 Form, I-9 Form, Fair Credit Reporting Act of 1970 Form, and DCC-101 form to Office Program Manager (PM)

- Report to the BOS, Office of Management to:
 - Review FDA 3391 Form
 - Must bring two original forms of identification (state issued photo ID, and one from the I-9 Form list)

- Once NCI has informed FDA Security Branch that Fellow clears security check, report to FDA Badging Office for badge issuance

- Report to FDA Personnel Security Branch with:
 - FDA 3391 Form
 - Two original forms of approved identification (**see above**)

- Satisfactorily completes all laboratory safety training requirements, if applicable

- Obtain appropriate training certifications for new fellows and annual recertification for:
 - Computer security
 - Economic espionage
 - Ethics training
- All Fellows in the Cancer Prevention program will participate in scientific and professional development activities of the NCI's Cancer Prevention Fellowship Program.

In order to participate in mentored regulatory review training:

- Complete the following documents
 - Confidential Financial Disclosure Report – **FTE fellows only** (must be updated on an annual basis)
 - Confidentiality Agreement for IOTF Fellows
 - Certification for Training – Conflict of Interest
 - FDA 2096 Form – Regulation Certification for New Employees (**FTE fellows only**)
 - FDA 2097 Form – Certification for Separating Employees (**FTE fellows only**)
 - HHS 520 Form – Request for Approval of Outside Activities, as applicable
- Forward completed forms (**see above**) to FDA Fellowship Program Manager
- Must receive notification by FDA Fellowship Program Manager, prior to commencement of mentored review training, that the Fellow's submitted "Conflict of Interest" (COI) information has been cleared by the FDA Division of Ethics and Security Branch

CBER Mentor/Sponsor:

- Adhere to all established policies and procedures set forth by CBER for the IOTF Fellowship Training Programs
- Post approved summaries of their projects on a web-based system developed by NCI/FDA so Fellows can select appropriate match
- Receive selected IOTF Fellow's name from the Associate Director for Training and Education, NCI
- Notifies the Personnel Liaison Specialists, Program Operations Branch, Division of Program Services, Office of Management (POB, DPS, OM) of selected IOTF Fellow's name
- Develop list of appropriate internal and external courses and training opportunities in consultation with the Fellow

- Forward “Training Plan” (is there an actual form used to develop the training plan?? (yes, NCI sends it directly to the Fellows for completion with the Mentor) to the Associate Director for Training and Education, NCI, once approved by Division/Office and Center Director or designee
- Ensures that Fellows are recused from reviewing any materials, engaging in proprietary meetings, or other proprietary activities relating to a financial interest that presents a “conflict of interest” as defined by FDA (**see Definitions**)
- Ensures Fellow successfully completes appropriate safety training requirements, if applicable
- Provide training in ongoing research projects and supervise all research activities
- Provide supervision, training, and mentoring in the relevant federal statutes, regulations, principles, and practices of FDA medical product review, including issues related to product development
- Encourage Fellows to participate in regulatory courses offered by various FDA Centers
- Submit reimbursable (**see section V, IOTF Program, Funding**) itemized expenses to Office of Management/Division of Planning, Evaluation, and Budget/Resource Management Branch (OM/DPEB/RMB) Administrative Officer responsible for IAGs through Division/Office Director and CBER’s Scientific Information Specialist, Office of the Center Director at the end of the second and fourth quarter of each fiscal year (i.e., end of March and September)

Office Program Manager (PM):

- Receive name of Fellow(s) and Mentor(s), with Fellow’s contact information from the Research Program Coordinator
- Contact Fellow(s) for appointment to fill out required forms
- Provide Fellow with required forms (**see Section VII, Forms Used**)
- Secures approval from Branch/Division/Office Directors, where applicable
- Enters appropriate information in EASE
- Requests a network account. Instructions on “How to Complete the Network Account Request Form” can be found at <http://intranet.fda.gov/cber/oitm/cmpnetac.htm>
 - All staff that utilize computers must take the FDA Security Awareness Training within 5 business days
 - All Fellowship network accounts will be set to expire on the “Not to Exceed” (NTE) date, set in the Enterprise Administrative Support Environment (EASE)

- Ensure Fellow and Mentor complete all forms and training
- Sends an email notification to the CBER Internal Exit Checkpoint prior to the Fellow's NTE date to initiate CBER's staff exit procedures.
- Maintains file for Fellow, to include all signed forms

Research Program Coordinator

- Receive Fellow's name and contact information from FDA IOTF Fellowship Program Manager
- Forwards Fellow's and Mentor's name, with contact information for Fellow to Office PMs

Personnel Liaison (PL) Specialists, Program Operations Branch, Division of Program Services, Office of Management (POB, DPS, OM):

- Enters name and appropriate information in EASE and GovTrip
- Advises Building Operations Staff, Office of Management (BOS) of Fellow's start and end dates.

Building Operations Staff, Office of Management (BOS/OM)

- Files copy of FDA 3398 Form

FDA IOTF Fellowship Program Manager

- Provide CBER Research Program Coordinator the names of the Fellow and Mentor, with contact information for the Fellow
- Receives completed COI/Confidentiality forms from Fellow
- Reviews COI information with the Office of Management Programs, Ethics and Integrity Staff (OMP/EIS)
- Notifies Fellow, mentor, and Research Program Coordinator when Fellow's COI information has been cleared by the OMP/EIS.
- Deals with identified conflicts on a case-by-case basis with Fellow and Mentor

Associate Director for Research, CBER

- Establishes policies and procedures for participation in the IOTF Fellowship Training Programs
- Signs all required forms

IX. Conditions for Acceptance

An IOTF Fellow: 1) May begin the training program if, a) all required forms are filled out and sent to the appropriate departments; b) CBER mentor is notified by the FDA Fellowship Program Manager (IOTF) of the Fellow's approved start date; 2) Can only work under the direct guidance of an appropriate CBER mentor or designee; and 3) Must meet all safety and security requirements, as applicable.

X. Extension of Appointment

The initial two year appointment, with the exception of fellowship opportunity #2, which is only a one year program, is the maximum a Fellow may spend at the FDA/CBER; thus no extensions of appointment are necessary.

XI. Termination of Appointment

An IOTF Fellow's appointment ends on the NTE date and all CBER/FDA related access cards and identification the Fellow possesses must be submitted to the mentor by the end of the appointment. An IOTF Fellow's appointment may be terminated prior to the NTE date, without prior notification, for a number of reasons, including but not limited to: 1) realignment or loss of resources; 2) concerns about the quality or productivity of the Fellow, or any other performance deficiency and/or inappropriate conduct.

XII. Contacts

Lisa Kable, Contract Liaison Officer, Office of Management/Division of Planning, Evaluation, and Budget/Resource Management Branch (OM/DPEB/RMB), 301-827-1414

Mary Poos, FDA Program Manager, Office of External Relations, (301-827-2825)

XIII. Effective Date

February 2008