Oncology Biologics Development Primer

February 28-29, 2008
Marriott Gaithersburg Washingtonian Center
Gaithersburg, MD

www.isbtc.org

Schedule at a Glance

Thursday, February 28

7:00 am – 8:00 am	*Breakfast*
8:00 am – 8:10 am	**Welcome and Introductions**
8:10 am – 8:55 am	**Keynote Address**
8:55 am – 10:25 am	**Session 1: PreClinical Development**
10:25 am – 10:40 am	*Break*
10:40 am – 12:30 pm	**Session 2: Clinical Development**
12:30 pm – 1:30 pm	*Lunch*
1:30 pm – 3:30 pm	**Session 3: Case Studies in Protein Therapeutics**
3:30 pm – 3:45 pm	*Break*
3:45 pm – 5:15 pm	**Session 4: Industry and Academic Relationships in Biologic Development**
5:15 pm – 6:30 pm	**Reception**

Friday, February 29

7:00 am – 8:00 am	*Breakfast*
8:00 am – 8:05 am	**Welcome and Overview**
8:05 am – 10:15 am	**Session 5: Regulatory Strategies in the Global Arena**
10:15 am – 10:30 am	*Break*
10:30 am – 12:00 pm	**Session 6: Case Studies in Vaccines**
12:00 pm – 1:00 pm	*Lunch*
1:00 pm – 2:40 pm	**Session 7: Case Studies in Cellular Therapeutics**
2:40 pm – 3:00 pm	*Break*
3:00 pm – 4:40 pm	**Session 8: Case Studies in Gene Therapies**
4:40 pm – 5:00 pm	**Closing Comments**

Thank You to Our 2008 Primer Supporters

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General Information

PRIMER OVERVIEW

iSBTc created the Oncology Biologics Development Primer (OBDP) to meet the needs of the biological therapy community by educating physicians and researchers on the worldwide regulatory paths for biological therapy development. Through facilitating collaborative interactions between regulators, preclinical scientists, clinical investigators and industry, the OBDP helped to ensure that active, innovative new therapies will be rapidly and appropriately moved into clinical testing.

The program was a key forum for continuing exploration and discussion of best practices for worldwide biologics development. Through the expertise of the invited speakers, panel members and course attendees, this rigorous and challenging program curriculum facilitated understanding, open discussion, and exploration of the development issues surrounding biologic agents for cancer.

INTENDED AUDIENCE

Physicians and scientists in academia, industry and regulatory agencies who have an interest in the strategic, preclinical, clinical and regulatory aspects of efficient oncology biologics development.

MEETING OBJECTIVES

- Provide a framework for dissemination of information for those actively involved in the development of biologic oncology therapeutics including discussion of new methodologies for best practices in preclinical testing and clinical trial design.
- Create a forum for dialogue among regulatory agencies, industry members and academic investigators regarding strategies for oncology biologics development.
- Encourage and enhance strategic thinking for oncology biologic therapeutics development by designing the preclinical and clinical development roadmap to achieve the desired goals.
- Gain an understanding of regulatory expectations and requirements in the development and approval process for oncology biologic therapeutics.

DESIRED OUTCOMES

- Understand where to find key informational resources and implement best practices regarding the development of oncology biological therapeutics.
- Form important relationships between regulatory agencies, industry members and academic investigators that result in effective strategies for oncology biologics development.
- Understand the concepts and processes for achieving the scientific and regulatory objectives by focusing both preclinical and clinical strategies to drive efficient development of oncology biologic therapeutics.
- Understand regulatory expectations and requirements and incorporate these ideas into the clinical trial design.

Program Schedule

Thursday, February 28

8:00 am – 8:10 am **Welcome and Meeting Introduction**
Robert J. Zimmerman, SD – Zimmerman Consulting (Program Organizer)

8:10 am – 8:55 am **Keynote Address**
Regulatory Overview of Oncology Biologics Product Development from Bench to First-in-Man
Raj Puri, MD, PhD – Food and Drug Administration

8:55 am – 10:25 am **Session 1: Preclinical Development**

8:55 am — Cell and Gene Therapy Products for Cancer Treatment
Ying Huang, PhD – Food and Drug Administration, CBER

9:20 am — Biological Therapeutics for Cancer Treatment
Andrew J. McDougal, PhD, DABT – Food and Drug Administration, CDER

9:45 am — Principles of Preclinical Development and Validation of Molecular Markers/Biomarkers of Toxicity and Efficacy for Cancer Therapies
Samir Khleif, MD – National Cancer Institute, CCR

10:10 am — Developing Biologics for Phase I Trials: Manufacturing and Toxicology Challenges
Anthony R. Welch, PhD – National Cancer Institute

10:40 am – 12:30 pm **Session 2: Clinical Development**

10:40 am — Phase I Design Issues: Surrogate Markers/Selecting Pts/Special Inclusion-Exclusion Criteria
Susan Jerian, MD – OncoRD, Inc.

11:20 am — Phase II and Beyond Issues
John M. Kirkwood, MD – University of Pittsburgh Cancer Institute

11:50 am — Good Clinical Research Practice – Working in the World of Regulated Research
Marta Fields – Amgen, Inc.

1:30 pm – 3:30 pm **Session 3: Case Studies in Protein Therapeutics**

1:30 pm — Cytokines: Lessons from Single Digit Cytokines IL2, IL7
Crystal Mackall, MD – National Cancer Institute, Pediatric Oncology

1:50 pm — Cytokines: Lessons from Double Digit Cytokines IL12, IL18 and Counting
Michael T. Lotze, MD – University of Pittsburgh Cancer Institute

2:10 pm — Antibodies: CTLA4 Antagonist Therapy for Cancer
Rachel Humphrey, MD – Bristol Myers-Squibb Company

2:30 pm — Antibodies: CD40 Agonist Development for Cancer
Robert Vonderheide, MD, D.Phil – University of Pennsylvania, Abramson Family Cancer Rsch Inst.

2:50 pm — Panel Discussion
Moderator: *Susan Jerian, MD – OncoRD, Inc.*

3:45 pm – 5:15 pm **Session 4: Industry & Academic Relationships in Biologic Development**

3:45 pm — Academic Drug Development: Bench to First-in-Man without Industry
Elizabeth Jaffee, MD – Johns Hopkins University

4:00 pm — Industry Perspective: What Industry Expects from Academic Partnerships
David R. Parkinson, MD – Nodality Inc.

4:15 pm — Academic Perspective: Role of Tech Transfer in Academia and Common Out-Licensing Criteria
Chris Moulding – USC Stevens Institute for Innovation

4:30 pm — Panel Discussion
Moderator: *Robert J. Zimmerman, SD – Zimmerman Consulting*

Program Schedule

Friday, February 29

8:00 am – 8:05 am **Welcome and Overview**
Robert J. Zimmerman, SD – Program Co-Organizer

8:05 am – 10:15 am **Session 5: Regulatory Strategies in the Global Arena**

8:05 am EU Perspective on Regulatory Issues for Biologics
Robert Charnas, PhD – Amgen, Inc.

8:40 am Japan Perspective on Regulatory Issues for Biologics
Ken Takeshita, MD – Celgene Corporation

9:15 am Clinical Trial Design Issues for Combination Products and Combination Therapies
Patricia Keegan, MD – Food and Drug Administration

9:45 am Panel Discussion
Moderator: *Robert J. Zimmerman, SD – Zimmerman Consulting*

10:30 am – 12:00 pm **Session 6: Case Studies in Vaccines**

10:30 am Dendritic Cell Based Vaccines:
Lothar H. Finke, MD – ARGOS Therapeutics

10:50 am Cancer Vaccines
Frederic Lehmann, MD – GlaxoSmithKline Biologicals s.a.

11:10 am Nucleic Acid Based Vaccines
Laurence Elias, MD – Geron Corporation

11:30 am Panel Discussion
Moderator: *Michael Lotze, MD – University of Pittsburgh Cancer Institute*

1:00 pm – 2:40 pm **Session 7: Case Studies in Cellular Therapeutics**

1:00 pm Overview of Adoptive Transfer T Cell Therapy for Cancer
Nicholas P. Restifo, MD – National Cancer Institute

1:20 pm NK Cell Therapeutics for Cancer
Jeffrey Miller, MD – University of Minnesota

1:40 pm Adoptive T Cell Transfer of Regulatory T Cells for GVHD
Carl H. June, MD – University of Pennsylvania

2:00 pm Mesenchymal Stem Cell Therapy with Prochymal™ for GVHD
C. Randal Mills, PhD – Osiris Therapeutics, Inc.

2:20 pm Panel Discussion
Moderators: *Carl H. June, MD – University of Pennsylvania*
C. Randal Mills, PhD – Osiris Therapeutics, Inc.

3:00 pm – 4:40 pm **Session 8: Case Studies in Gene Therapies**

3:00 pm Oncolytic Viruses: Reovirus
Matt Coffey, PhD – Oncolytics Biotech, Inc.

3:20 pm Gene Modified T Cell Therapy
Michel Sadelain, MD, PhD – Memorial Sloan-Kettering Cancer Center

3:40 pm Adenovirus Vectors
Sunil Chada, PhD – Introgen Therapeutics, Inc.

4:00 pm Panel Discussion
Moderator: *Mercedes Serabian, MS, DABT – Food and Drug Administration, CBER*

4:40 pm – 5:00 pm **Closing Comments**
Robert J. Zimmerman, SD – Program Co-Organizer

Primer Faculty

Organizing Committee

Susan Jerian, MD *
OncoRD, Inc.

Carl H. June, MD *
University of Pennsylvania

Mercedes Serabian, MS, DABT
Food and Drug Administration, CBER

Robert J. Zimmerman, SD
Zimmerman Consulting

Faculty

Sunil Chada, PhD
Introgen Therapeutics, Inc.

Robert Charnas, PhD
Amgen, Inc.

Matt Coffey, PhD
Oncolytics Biotech, Inc.

Laurence Elias, MD
Geron Corporation

Marta Fields
Amgen, Inc.

Lothar H. Finke, MD
ARGOS Therapeutics

Ying Huang, PhD
Food and Drug Administration, CBER

Rachel W. Humphrey, MD
Bristol-Myers Squibb Company

Elizabeth M. Jaffee, MD
Johns Hopkins University

Susan Jerian, MD *
OncoRD, Inc.

Carl H. June, MD *
University of Pennsylvania

Patricia Keegan, MD
Food and Drug Administration

Samir Khleif, MD
National Cancer Institute, CCR

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University of Pittsburgh Cancer Institute

Frederic Lehmann, MD
GlaxoSmithKline Biologicals s.a.

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University of Pittsburgh Cancer Institute

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Food and Drug Administration

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Memorial Sloan-Kettering Cancer Center

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Food and Drug Administration, CBER

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Celgene Corporation

Robert H. Vonderveide, MD, D.Phil
University of Pennsylvania, Abramson Family Cancer Rsch. Inst.

Anthony R. Welch, PhD
National Cancer Institute

Robert J. Zimmerman, SD
Zimmerman Consulting

* Note: The faculty marked with an asterisk have indicated a financial relationship with Merck & Co., Inc., a supporter of this program.

US Reference Materials

CMC

1. **Content and Review CMC Guidance for Human Gene Therapy Investigational New Drug Applicants (INDs)** *(November 2004)*
   http://www.fda.gov/cber/gdlns/gtindcmc.htm

2. **Instructions and Template for CMC Reviewers of Human Somatic Cell Therapy Investigational New Drug Applications (INDs)** *(August 2003)*
   http://www.fda.gov/cber/gdlns/cmcsomcell.htm

3. **Supplemental Guidance on Testing for Replication Competent Retrovirus in Retroviral Vector Based Gene Therapy Products and During Follow-Up of Patients in Clinical Trials Using Retroviral Vectors** *(November 2006)*
   http://www.fda.gov/cber/gdlns/retrogt1000.htm

4. **Points to Consider in the Manufacture and Testing of Monoclonal Antibody Products for Human Use** *(February 1997)*
   http://www.fda.gov/cber/gdlns/ptc_mab.pdf

Pre-Clinical

1. **Guidance for Industry: S6 Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals** *(July 1997; ICH)*
   http://www.fda.gov/cder/guidance/1859fnl.pdf

2. **Guidance for Industry: Guidance for Human Somatic Cell Therapy and Gene Therapy**
   http://www.fda.gov/cber/gdlns/somgene.htm

Clinical

1. **Gene Therapy Clinical Trials – Observing Subjects for Delayed Adverse Events** *(November 2006)* - CBER Long-Term Follow-up for Gene Therapy Trials
   www.fda.gov/cber/gdlns/gtclin.html

2. **Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics** *(May 2007)* - Oncology Endpoints (CDER)
   www.fda.gov/cder/guidance/7478fnl.htm

3. **Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products** *(May 1998)*
   http://www.fda.gov/cder/guidance/1397fnl.pdf

4. **FDA Approval of New Cancer Treatment Uses for Marketed Drug and Biological Products** *(December 1998)*
   http://www.fda.gov/cder/guidance/1484fnl.htm

5. **Estimating the Maximum Safe Starting Dose in Initial Clinical Trials for Therapeutics in Adult Healthy Volunteers** *(July 2005)*
   http://www.fda.gov/cder/guidance/5541fnl.htm

6. **Exploratory IND Studies** *(July 2006)*
   http://www.fda.gov/cder/guidance/7086fnl.htm

US Reference Materials

Clinical *(continued)*

7. **AE (Adverse Event) Reporting – Improving Human Subject Protection** *(April 2007)*
   http://www.fda.gov/cber/gdlns/advreport.pdf

8. **Establishment and Operation of Clinical Trial Data Monitoring Committees** *(March 2006)*
   http://www.fda.gov/cber/gdlns/clintrialdmc.htm

GCP Reference Material

1. **Code of Federal Regulations Title 21 Part 312 – Investigational New Drug Application**
   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312

2. **Code of Federal Regulations Title 21 Part 50 – Protection of Human Subjects**
   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50

3. **Code of Federal Regulations Title 21 Part 54 – Financial Disclosure by Clinical Investigators**
   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=54

4. **Code of Federal Regulations Title 21 Part 56 – Institutional Review Boards**
   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56

5. **International Conference on Harmonisation – E6 Good Clinical Practice; Consolidated Guidance**
   http://www.fda.gov/cder/guidance/959fnl.pdf

6. **DRAFT Guidance for Industry: Protecting the Rights, Safety, and Welfare of Study Subjects – Supervisory Responsibilities of Investigators**
   http://www.fda.gov/OHRMS/DOCKETS/98fr/07d-0173-gdl0001.pdf

7. **FDA Information Sheet: FDA Inspections of Clinical Investigators**
   http://www.fda.gov/oc/ohrt/irbs/investigator.pdf

Regulatory

1. **Fast Track 2004**
   http://www.fda.gov/cder/guidance/5645fnl.htm

2. **Phase I**
   http://www.fda.gov/cder/guidance/clin2.pdf

3. **QT/QTc testing**
   http://www.fda.gov/cder/guidance/6922fnl.htm

4. **Target Product Profile**
   http://www.fda.gov/cder/guidance/6910dft.htm

5. **FDA – 1572 Form**
   http://www.fda.gov/opacom/morechoices/fdaforms/FDA-1572.pdf

US Reference Materials

Regulatory *(continued)*

6. **1571 ES** – FDA – Investigational New Drug Application (IND)
   http://www.fda.gov/opacom/morechoices/fdaforms/1571es.pdf

7. **3500 MedWatch Form** – The FDA Safety Information and Adverse Event Reporting Program
   http://www.fda.gov/medwatch/safety/3500.pdf

8. **3500A MedWatch Form**
   http://www.fda.gov/medwatch/safety/3500a.pdf

9. **IND Meetings for Human Drugs and Biologics (FDA)**
   www.fda.gov/cder/guidance/3683.fnl.htm

10. **Guidance for Industry – Formal Meetings with Sponsors and Applicants for PDUFA Products** *(February 2000)*
    http://www.fda.gov/cder/guidance/2125fnl.htm

11. **Part 11, Electronic Records; Electronic Signatures – Scope and Application** *(August 2003)*
    http://www.fda.gov/Cder/guidance/5667fnl.htm

EU Reference Materials

European Legislation

1. **EUDRALEX – The Rules Governing Medicinal Products in the European Union**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/index.htm

2. **Regulation on Advanced Therapy**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2007_1394/reg_2007_1394_en.pdf

3. **Updated Regulation on the EMEA and Pharmacovigilance**
   http://ec.europa.eu/enterprise/pharmaceuticals/review/doc/final_publ/reg_2004_726_20040430_en.pdf

4. **Updated Directive on Human Medicinal Products**
   http://ec.europa.eu/enterprise/pharmaceuticals/review/doc/final_publ/dir_2004_27_20040430_en.pdf

5. **Clinical Trials Directive**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2001_20/dir_2001_20_en.pdf

6. **Directive on Investigational Medicinal Products and Importation**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2005_28/dir_2005_28_en.pdf

7. **Directive – GMP Requirement for Human Medicinal Products**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdf

8. **Orphan Medicinal Products**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf

9. **Criteria for Orphan Medicinal Products**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2000_847/reg_2000_847_en.pdf

10. **Payment of Fees to, and the Receipt of Administrative Assistance from, the European Medicines Agency by Micro, Small and Medium-Sized Enterprises.**
    http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2005_2049/reg_2005_2049_en.pdf

11. **Regulation on Pediatric Development**
    http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1901/reg_2006_1901_en.pdf

12. **Regulation (EC) No 1902/2006 of the European Parliament and of the Council of 20 December 2006 amending Regulation 1901/2006 on Medicinal Products for Pediatric Use**
    http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/reg_2006_1902/reg_2006_1902_en.pdf

13. **Genetically Modified Organisms in the Environment**
    http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2001_18/dir_2001_18_en.pdf

EU Reference Materials

European Legislation *(continued)*

14. ***Volume 10 of Eudralex Devoted to Clinical Trial legislation***
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev10.htm

Chapter I: Application and Application Form

1. **Guidance on Clinical Trial Application, Notification of Substantial Amendments and Declaration of the End of the Trial**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/11_ca_14-2005.pdf

2. **Ethics Committee Application**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/12_ec_guideline_20060216.pdf

3. **Guidance on the EUDRACT Data Base**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/13_cp_and_guidance_eudract_april_04.pdf

Chapter II: Monitoring and Pharmacovigilance

1. **Guidance on Collection, Presentation and Verification of AE Reports from Clinical Trials**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/21_susar_rev2_2006_04_11.pdf

2. **Guidance on EU Database on SUSARs**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/22_cp_and_guidance_database_susars16_april_2004.pdf

Chapter III: Quality of Investigational Medicinal Products

1. **Good Manufacturing Practices**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-4/pdfs-en/an13final_24-02-05.pdf

2. **Annex 13 to Good Manufacturing Practices**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-4/pdfs-en/an13final_24-02-05.pdf

3. **EU Format for Manufacturing Authorization**
http://www.emea.europa.eu/Inspections/GMPCompproc.html
http://www.emea.europa.eu/Inspections/docs/CoCP/CoCP_FormatMA.pdf

4. **GMP Status of Manufacturers in Third Countries**
http://www.emea.europa.eu/Inspections/docs/CoCP/CoCP_VerificationGMP3rdCountry.pdf

5. **Guideline: Quality Requirements for Investigational Medicinal Products in Clinical Trials**
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/18540104en.pdf

EU Reference Materials

Chapter V: Additional Information

1. **Content of Trial Master File and Archiving**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/v10_chap5.pdf

2. **Q & A – Clinical Trial Documents**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/v10_chap5.pdf

3. **Guidance on Investigational Medicinal Products for Clinical Trials**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-10/guidance-on-imp_nimp_04-2007.pdf

Chapter VI: Legislation

1. **Manufacture and Importation of Investigational Medicinal Products**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-1/dir_2005_28/dir_2005_28_en.pdf

2. **Marketing Authorization – Notice to Applicants**
   http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm

UK Links – MHRA and others

1. **Electronic Medicines Compendium**
   http://emc.medicines.org.uk

2. **Clinical Trials**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=101

3. **Applying for a Clinical Trial Application**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=723

4. **Maintaining a Clinical Trial Application**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=983

5. **Making Clinical Trial Applications**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=1123

6. **Additional Information**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=1177

7. **Fees for Clinical Trials**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=1124

8. **Forms for Clinical Trials**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=1125

9. **Safety Reporting – Annual Safety Reports and SUSARs**
   http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=993

EU Reference Materials

General Information

1. **EudraPharm –** A source for all medicinal products in Europe
   http://eudrapharm.eu/eudrapharm/welcome.do?selectedStaticLocale.languageCode=en

2. **Heads of Agencies**
   http://www.hma.eu/index.html

3. **French Agency – AFSSAPS** *(English Language Link)*
   http://agmed.sante.gouv.fr/ang/indang.htm

4. **List of Ongoing Clinical Studies in France** *(in French)*
   http://agmed.sante.gouv.fr/htm/5/repec/repec0.htm

5. **Medical Products Agency** *(Sweden site in English)*
   http://www.lakemedelsverket.se/Tpl/NormalPage____2159.aspx

6. **Danish Medicines Agency – Legislation** *(English)*
   http://www.dkma.dk/1024/visUKLSArtikel.asp?artikelID=742

Guidelines

1. **Link to CHMP Efficacy and Safety Guidelines**
   http://www.emea.europa.eu/htms/human/humanguidelines/efficacy.htm

2. **Pharmacokinetics of Therapeutic Proteins**
   http://www.emea.europa.eu/pdfs/human/ewp/8924904enfin.pdf

3. **Evaluation of Anticancer Medicinal Products in Humans**
   http://www.emea.europa.eu/pdfs/human/ewp/020595en.pdf

4. **Annual Safety Report Template** – an example
   www.ucl.ac.uk/biomed-r-d/guides/guide_asrprep_submission.doc

5. **Radiation Protection**
   http://ec.europa.eu/energy/nuclear/radioprotection/doc/legislation/9629_en.pdf
   http://ec.europa.eu/energy/nuclear/radioprotection/doc/legislation/9743_en.pdf

6. **Radiation Protection – UK Specific Legislation**
   http://www.corec.org.uk/applicants/apply/docs/Question-specific_Guidance.doc
   http://www.corec.org.uk/applicants/docs/NHS_REC_Application_Form_v5_Content_Changes.doc

7. **EMEA – Guideline on Adjuvants in Vaccines for Human Use** *(January 2005)*
   http://www.emea.europa.eu/pdfs/human/vwp/13471604en.pdf

8. **EMEA – Guideline on Strategies to Identify and Mitigate Risks for First-in-Human Clinical Trials with Investigational Medicinal Products** *(July 2007)*
   www.eanm.org/news/doc_infoc/EMEA_Guideline_First_In_Man_Clinical_Trials_07_2007.pdf

Japan Reference Materials

1. "**Drug Approval and Licensing Procedures in Japan 2005**" Published by Jiho Co., Tokyo (ISBN 4-8407-3649-9)
   The most recent official English translation of the industry "Bible" in Japan. The Pharmaceutical Affairs Laws have not changed substantially with respect to biologics since 2005.

2. **Commercialization of Pharmaceutical and Biologics Research: Regulations You Should Know** *(website)* - Contains links to Japanese language documents describing in fairly simple terms the preclinical and clinical regulations on biologics.
   http://www.nibio.go.jp/guide/index.htm

3. **Kitasato University-Harvard School of Public Health Symposium Home Page** *(website)* – Contains useful English and Japanese language slide presentations by various experts in the general field of pharmaceutical industry and drug development.
   http://www.pharm.kitasato-u.ac.jp/biostatis

4. **Biologics Forum** *(Japanese-language website)* – Group that hosts an annual meeting on biologics. Contains links to useful PowerPoint presentations in both English and Japanese.
   http://www.nihs.go.jp/dbcb/Biologics_forum/bioforum-top.html

Additional Reference Materials

Journal Articles, Papers, Editorials

1. **Preclinical Safety Testing of Monoclonal Antibodies: The Significance of Species Relevance** by Kathryn Chapman, Nick Pullen, Mark Graham and Ian Ragan
   Published in: *Nature Reviews Drug Discovery,* Vol 6, February 2007, pp 120-126.

2. **Safety Assessment of Biotechnology-Derived Pharmaceuticals: ICH and Beyond**
   by Mercedes Serabian and Anne Pilaro
   http://www.toxpath.org/stp_journal_archive/VOL%2027,%20NO%201,%20PART%20NA,%201999.PDF
   Published in: *Toxicology Pathology,* Vol 27, No 1, 1999, pp 27-31.

3. **Preclinical Development Strategies for Novel Gene Therapeutic Products**
   by Anne Pilaro and Mercedes Serabian
   http://www.toxpath.org/stp_journal_archive/VOL%2027,%20NO%201,%20PART%20NA,%201999.PDF
   Published in: *Toxicology Pathology,* Vol 27, No 1, 1999, pp 4-7.

4. **Use of Nontraditional Animals for Evaluation of Pharmaceutical Products** by Abigail Jones
   Opinion piece. Published in: *Informa Healthcare,* 2006

5. **Understanding and Applying Regulatory Guidance on the Nonclinical Development of Biotechnology-Derived Pharmaceuticals** by David Snodin and Peter Ryle
   Published in: B*iodrugs*, Vol 20, 2006, pp 25-52.

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   Published in: Elsevier's *Clinical Reviews in Oncology Hematology,* 2007, pp 34-42.

7. **Points to Consider Regarding Safety Assessment of Biotechnology-Derived Pharmaceuticals in Non-Clinical Studies** (English Translation) by Takahiro Nakazawa, Shuichi Kai, Mutsufumi Kawai, Eiji Maki, Fumio Sagami, Hiroshi Onodera, Satoshi Kitajima and Tohru Inoue
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8. **Preclinical Safety Evaluation of Monoclonal Antibodies** by Roly Foulkes
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9. **A Clinical Development Paradigm for Cancer Vaccines and Related Biologics** by Hoos A, Parmiani G, Kristen H, Sznol M, Loibner H, Eggermont A, Urba W, Blumenstein B, Sacks N, Keilholz U, Nichol G for the Cancer Vaccine Clinical Trial Working Group
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10. **Phase I Trial Design for Solid Tumor Studies of Targeted, Non-Cytotoxic Agents: Theory and Practice** by Parulekar W and Eisenhauer E
    Published in: *Journal of the National Cancer Institute*, Vol 96, No 13, 2004, pp 990-97.

11. **Non-Toxicity Endpoints in Phase I Trial Designs for Targeted, Non-Cytotoxic Agents** by Korn E
    Published in: *Journal of the National Cancer Institute*, Vol 96, No 13, 2004, pp 977-8.

Additional Reference Materials

Journal Articles, Papers, Editorials *(continued)*

12. **Anticancer Agents Targeting Signaling Molecules and Cancer Cell Environment: Challenges for Drug Development?** by Gelman K, Eisenhauer E, Harris A, Ratain M, Workman P
Published in: *Journal of the National Cancer Institute*, Vol 91, No 15, 1999, pp 1281-7.

13. **Recommended Changes to Oncology Clinical Trial Design: Revolution or Evolution?** by Ratain M, Humphrey R, Gordon G, Fyfe G, Adamson P, Fleming T, Stadler W, Berry D, Peck C
Published in: *European Journal of Cancer*, Vol 44, 2008, pp 8-11.

14. **Prognostic Significance of Autoimmunity During Treatment of Melanoma with Interferon** by Gogas H, Iannovich I, Dafni U, Stavropoulou-Giokas C, Frangia K, Tsoutsos D, Panagiotou P, Polyzos A, Papadopoulous O, Stratigos A, Markopoulos C, Bafaloukos D, Pectasides D, Fountzilas G, Kirkwood, J.
Published in: *New England Journal of Medicine*, Vol 354, No 7, February 2006, pp 709-18.

15. **Meta-Analysis of Phase II Cooperative Group Trials in Metastatic Stage IV Melanoma to Determine Progression Free and Overall Survival Benchmarks for Future Phase II Trials** by Korn E, Liu P, Lee S, Chapman J, Niedzwiecki D, Suman V, Moon J, Sondak V, Atkins M, Eisenhauer E, Parulekar W, Markovic S, Saxman S, Kirkwood J.
Published in: *Journal of Clinical Oncology,* Vol 26, No 4, February 2008, pp 527-34.

16. **A Pooled Analysis of Eastern Cooperative Oncology Group and Intergroup Trials of Adjuvant High-Dose Interferon for Melanoma** by Kirkwood J, Manola J, Ibrahim J, Sondak V, Ernstoff M, Rao U.
Published in: *Clinical Cancer Research*, Vol 10, 2004, pp 1670-77.

17. **Prospect of Targeting the CD40 Pathway for Cancer Therapy** by Vonderheide R
Published in: *Clinical Cancer Research,* Vol 13, No 4, 2007, pp 1083-88.

18. **Interleukin Therapy** by Lotze MT
Published in: DeVita, Hellman, and Rosenberg's *Cancer: Principles and Practice of Oncology* by Vincent T. DeVita, Theodore S. Lawrence, Steven A. Rosenberg, Robert A. Weinberg, and Ronald A. DePinho, Lippincott Williams & Wilkins, Philadelphia, 2008.

19. **Guidelines for Assuring the Quality and Non-Clinical Safety Evaluation of DNA Vaccines**
World Health Organization, 2005
http://www.who.int/biologicals/publications/ECBS%202005%20Annex%201%20DNA.pdf

Additional Reference Materials

Websites to Consider for Bench to Beside Development of New Agents

1. **Clinical and Translational Science Awards** (CTSA) is a national consortium funded through Clinical and Translational Science Awards to transform how clinical and translational research is conducted. www.ctsaweb.org.

2. **Developmental Therapeutics Program at the NCI/NIH** has a number of grants and contracts programs that provide support for various stages of new drug development from preclinical feasibility and toxicology support to the production of clinical grade reagents including IND filing assistance (Rapid Access to Interventional Development (RAID)) program. www.dtpnci.nih/gov.

3. **Financial Conflict of Interest** is an increasingly important issue to consider when intellectual property is licensed to biotechnology or pharmaceutical companies for clinical development. The American Association of Medical Colleges (AAMC) provides guidelines for investigators that have been adopted by many Universities for use by University Conflict of Interest Committees that manage these conflicts. These guidelines can be found at: www.AAMC.org/research/COI/.

Other Resources *(as taken from the presentation of Dr. Raj Puri)*

1. **Biological Product – Information on Submitting an Investigational New Drug Application** http://www.fda.gov/cber/ind/ind.htm

2. **Investigational New Drug (IND) Guidances**. http://www.fda.gov/cber/ind/indpubs.htm

3. **Cellular and Gene Therapy Publications** where you can find draft gene therapy guidance document and draft somatic cell therapy document. http://www.fda.gov/cber/genetherapy/gtpubs.htm

4. **Guidance for Industry – E6 Good Clinical Practice: Consolidated Guidance** *(April 1996)* http://www.fda.gov/cder/guidance/959fnl.pdf

5. **Summary ICH Workshop on Oncolytic Viruses and Future ICH Considerations Paper**: www.ICH.org, Gene Therapy Discussion Group

6. **Interagency Oncology Task Force – Joint Fellowship Training Program Information** http://iotftraining.nci.nih.gov/index.html

7. **FDA's Critical Path Initiative**: http://www.fda.gov/oc/initiatives/criticalpath/

8. **FDA, NCI, and CMS Collaboration- Oncology Biomarker Qualification Initiative (OCBI)** – Information on the collaboration/initiative through the press release: http://www.fda.gov/bbs/topics/news/2006/NEW01316.html

9. **The Biomarkers Consortium** - A joint venture of FNIH-NIH-FDA-Academia-Industry. An endeavor to discover, develop, and qualify biological markers (biomarkers) to support new drug development, preventative medicine, and medical diagnostics. www.biomarkerconsortium.org

2008 iSBTc Educational Program Preview

Primer on Tumor Immunology and Biological Therapy of Cancer

October 30, 2008 ~ San Diego, CA

This primer will provide a current overview of immunology as it applies to cancer etiology, biology and therapy. The target audience for this program is basic and clinical investigators from academic, regulator, and biopharmaceutical venues. The audience includes clinicians, researchers, students, post-doctoral fellows and allied health professionals.

Topics to be Addressed:

- Adoptive T Cell Therapy
- Anti-Angiogenic Therapies
- Antibody Therapy of Cancer
- Approach to Identification and Therapeutic Exploitation of Tumor Antigens
- Blocking Anti-T Cell Checkpoints
- Cytokines
- Immune Adjuvants
- Immune Monitoring of Cancer Immunotherapy
- Mechanisms of Immune-mediated Tumor Lysis
- T Reg Cells

Program Objectives:

- Provide a current overview of immunology as it applies to cancer etiology, biology, and therapy.
- Present in-depth concepts of cellular immunology and the host-tumor-immune system interactions.
- Present in-depth concepts of humorally-based immune therapies
- Present in-depth concepts of cytokine biology and role in cancer therapy
- Educate the audience regarding the foundation and methods for clinical trials of biologic / immunologic topics

Expected Outcomes: Attendees will learn the current status and the most recent advances in biologic therapies including cancer vaccines, vaccine adjuvants, host-tumor interactions and the role of the innate and adaptive immune systems in tumor immunology and therapy.

Organizers: Patrick Hwu, MD - *MD Anderson Cancer Center*
Kim Margolin, MD - *City of Hope*

Workshop on Inflammation in Cancer Development

October 30, 2008 ~ San Diego, CA

This small group, interactive workshop will assemble thought-leaders in the field to discuss inflammation and its role in cancer with an expected results publication following the program.

Meeting Features: Small group, interactive settings; Expert lectures; Breakout sessions; Held in conjunction with the iSBTc Annual Meeting

Organizers: Lisa M. Coussens, PhD – *University of California, San Francisco*
Steve Dubinett, MD – *University of California, Los Angeles*
Michael Karin, PhD – *University of California, San Diego*
George Weiner, MD – *University of Iowa*

2008 iSBTc Educational Program Preview

iSBTc 23rd Annual Meeting

October 31 – November 2, 2008 ~ San Diego, CA

The iSBTc Annual Meeting facilitates exchange of the most cutting edge preclinical and clinical data on the use biological therapies in cancer between basic scientists and clinicians from academic, regulatory and industrial venues. This meeting will allow various investigators to share and build on their data, ultimately leading to better patient outcomes in cancer.

Topics to be Addressed:

- Adoptive Transfer
- Cancer Stem Cells and the Host Response
- Endpoints, Response Criteria for Clinical Trial Design
- Enhancing Cancer Vaccines
- Innate Immunity to Tumors
- TH-17, Cytokines and T Cell Subsets
- Tumor Escape / Tumor Microenvironment
- Tumor Targeting Monoclonal Antibodies

Intended Audience: The target audience for the Annual Meeting includes both basic and clinical investigators involved in cancer research comprising members of academic, pharmaceutical and regulatory agencies. Attendees will include basic scientists, clinicians, graduate students, and post-doctoral fellows, as well as other allied health professionals.

Program Objectives:

- Promote scientific exchange of most recent advances and data in the biological treatment of cancer, as well as advances in basic cancer biology with relevance for anti-tumor immunity
- Promote the generation of new ideas incorporating these advances and explore their potential for impact on treatment outcomes
- Discuss the latest clinical developments regarding application of biologic approaches and establish dialogue between academic, government, and industry regarding implications as well as future directions
- Educate and provide perspective to the audience on the broad range of scientific developments in cancer and biological approaches to therapy
- Discuss current approaches to immunological monitoring
- Discuss current regulatory guidelines and how they impact clinical trials as well as resource availability

Organizers: Thomas A. Davis, MD - *Celldex Therapeutics, Inc.*
Thomas F. Gajewski, MD, PhD - *University of Chicago*
William J. Murphy, PhD - *University of Nevada*
Hideaki Tahara, MD, PhD - *University of Tokyo*

Webinar

"Primer on Tumor Immunology and Biological Therapy"

The free iSBTc webinar, "Primer on Tumor Immunology and Biological Therapy" is now available for viewing at the iSBTc website, www.isbtc.org, as well as for purchase on CD-ROM. This Primer provides an overview of tumor immunology and biological therapy by leaders in the field to educate viewers on both the biologic underpinnings of the field, as well as recent basic science and clinical developments. This webinar was created from the live program that was held in conjunction with the iSBTc 22nd Annual Meeting in Boston, MA.

The webinar consists of video-taped presentations by each speaker synchronized to their slide-set as it appeared during the program. This webinar will be available online through 2008. A CD-ROM of this program is available for a minimal fee. By purchasing the CD, you'll be able to keep this valuable tool and view it at anytime.

For more information about these upcoming iSBTc programs, please visit www.isbtc.org.

About iSBTc

The International Society for Biological Therapy of Cancer (iSBTc) was established in 1984 to facilitate the exchange and promotion of scientific information about the use of biological cancer therapies. The iSBTc defines biological cancer therapies as those based on host response mechanisms used to control or prevent tumor growth. The iSBTc is a 501 (c)(3) not for profit organization of medical professionals with a constituency of academic, government, industry, clinical, and basic scientists from around the world. The Society was founded on the belief that new systemic therapeutic treatments would continue to complement chemotherapies and move into the mainstream in the fight against cancer. To aid in this effort, iSBTc provides channels for the constructive discussion of current clinical trial results and methodologies, as well as a means to collaborate on new initiatives in tumor immunology and biological therapy. It is these key interactions and innovations that help advance the progress of cancer research and therapies and ultimately lead to better patient outcomes.

iSBTc Core Purpose

To improve cancer patient outcomes by advancing the development and application of biological therapy.

iSBTc Core Values

- **Interaction** – exchange of information and education among basic researchers and clinicians
- **Innovation** – development and application of biological therapy; seeking the best research and thinking related to the Society's purpose and vision
- **Leadership** – defining what is new and important

Disease States

iSBTc programming and membership covers the full spectrum of both solid tumors and hematologic malignancies including:

- Breast
- Colorectal
- Head & Neck
- Hepatocellular
- Kidney
- Leukemia
- Lung
- Lymphoma
- Melanoma
- Neuroblastoma
- Ovarian
- Prostate
- Renal Cell

Medical Specialties

iSBTc members and delegates represent many areas of biological science including:

- Cell Biology
- Dermatology
- Genetics
- Gynecologic Oncology
- Hematology
- Immunotherapy
- Internal Medicine
- Medical Oncology
- Microbiology
- Molecular Biology
- Pediatric Oncology
- Pharmacology / Toxicology
- Radiation Oncology
- Radiology
- Stem Cell Biology
- Surgical Oncology
- Transplantation

International Society for Biological Therapy of Cancer
555 E. Wells Street, Ste 1100, Milwaukee, WI 53202
Ph: 414-271-2456 ~ Fax: 414-276-3349
www.isbtc.org ~ info@isbtc.org

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