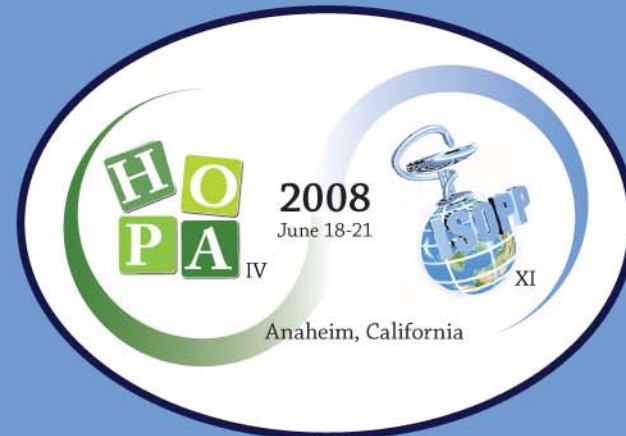


Getting Started in Practical Pharmacy Research



Paul R. Hutson, PharmD, BCOP
Associate Professor
University of Wisconsin School
of Pharmacy
Madison, Wisconsin

Disclosure

- Paul Hutson, PharmD, BCOP has received research grants from Baxter Healthcare and Millennium Pharmaceuticals

So ...

- What is “practical pharmacy research”?
- And why do you want to be doing it?

Fundamental Self-Assessment

- Do I want to be:
 - The innovator?
 - The person in charge of the study?
 - Extending this line of research into the foreseeable future (vs one-time question)?
- Vs
 - A facilitator
 - An integral member of the research team

Why Do You Want to Do “Research”?

- Innate curiosity
- Improve patient care in short and long term
- Problem-solving nature based upon clinical experiences and events
- Move into an academic position
- Improve professional image and credibility
- Increase salary

What Is Research?

- Is it new knowledge or methods presented in a scholarly venue?
 - Poster session or platform presentation
 - Regional
 - National
 - International
 - Peer-reviewed scholarly journal
 - Pharmacy focused
 - Hematology/oncology focused

What Kind of Scholarly Work Would You Like to Do? Is it Research?

- Case report
- Case series
- Clinical trial
 - Open-label intervention
 - Randomized, double-blind, placebo-controlled
 - Cooperative group liaison
 - Investigational Drug Service
- Animal and/or laboratory-based research

Scholarly Work vs Research

- What distinction is made between these 2 terms?
- Most commonly,
 - Scholarly work is the generation of new knowledge or methods, and its integration into new understanding or applications (Weiser 1996)
 - <http://www.cals.vt.edu/facultystaff/evaluation/scholarlyactivitydefinition.html>
 - Weiser, C. J., The Value System of A University- Rethinking Scholarship
<http://www.adec.edu/clemson/papers/weiser.html>

Scholarly Work vs Research

- How is “research” defined?

“Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.”

Scholarly Work vs Research

- Inductive research
 - Not hypothesis-based
 - Exploratory, hypothesis-generating
 - Often local or corporate funding used
- Hypothesis-driven research
 - Most common form in competitive grant proposals
 - Eg, “Palms and soles to which BAN antiperspirant has been applied will not have more or less hand/foot syndrome from capecitabine than untreated palms and soles” (null hypothesis)

Do You Want to Run or Share a Lab?

- Pharmacokinetics (PK)
- Pharmacogenomics/translational correlates
- Overhead (in addition to training)
 - Usually requires at least 1 technician
 - One vs multiple projects
 - Cost center/budget demands
 - Typically in major cancer centers

About That Training ...

- Most PK/PD lab directors have either or both a graduate degree or research fellowship with the intent of developing:
 - Analytical instrumentation skills
 - Writing skills
 - Grant
 - Protocol
 - Manuscript
 - Immersion in the research milieu

Big Lab People

- Wisconsin – Jill Kolesar
- Tennessee
 - Mary Relling
 - Sharyn Baker, Alex Sparreboom
- Missouri – Howard McLeod
- Nevada – Burgess Freeman
- Pennsylvania – Reggie Frye
- Maryland – W. Doug Figg

Big Lab Context

- Typically fellowship training
 - Laboratory skill development
 - Research interest germination
 - Grant and manuscript writing mentorship
- Typically located at big cancer centers
 - Usually supported by RO1 and UO1 funding
 - ± Graduate student or fellow training
 - Lab equipment and staff bootstrapping

Big Lab Opportunities

- Big labs often have staffing depth and scope of projects to permit and encourage mini sabbaticals for the purpose of:
 - Learning specific lab skills
 - Learning about advanced clinical trial management and operations
 - Advanced mentorship
 - PharmD
 - Physician
 - Study coordinating staff and regulatory

Animal-Based Research

- Advantages include:

- Decreased cost
- Easier recruitment and consenting
- Controlled conditions

- Disadvantages include:

- Acquisition and housing costs are real
- Requires animal handling facilities and training
- Limited sampling possibilities (volume and number)

Animal Research Options

- Find a contact:
 - On-/off-site veterinary school
 - On-site research animal training office
 - You are seeking guidance and training in:
 - Regulations and animal use guidelines
 - Appropriate species, strains, age, and sex
 - Appropriate facilities
 - Study and animal appropriate measurements
 - Handling, anesthesia, surgical procedures
 - Euthanasia and disposal

Controlled Clinical Trials

- Do you want to design protocols?
 - Identification of hypothesis to be tested
 - Identification of collaborators
 - Prescribing physician
 - Research nurse and/or data managers
 - Biostatistician
 - Preparation of grant
 - Resubmission of grant
- Do you want to help implement protocols?

Controlled Clinical Trials

- Once your hypothesis is identified ...
 - Discuss with MD and statistician (if needed)
 - Present concept to collaborating staff
 - Group physicians
 - Study nurses and data managers
 - Get buy-in and suggestions
 - Prepare protocol
 - Identify funding source (or donated drug)
 - Prepare your paperwork (ugggh!)

The Paperwork

- Protocol
- Grant application
- IRB (human subjects) application
- HIPAA application
- Data collection forms (CRFs)
- And, if needed ...
 - CTRC (old GCRC) application
 - IND application (if needed)

ALCAR for CIPN Prevention

- Original concept was to use memantine to prevent oxaliplatin-induced peripheral neuropathy
 - Literature review suggested better preliminary data in animal model and anecdotal human experience with acetyl-L-carnitine (ALCAR)
- Prepared a concept presentation
 - GI group wasn't interested (why not?)

ALCAR for CIPN Prevention

- Presented concept to 2 other groups, with input from biostatistician
 - Gyn/Onc (paclitaxel + carboplatin in IVIP treatment of ovarian cancer)
 - Hematology (bortezomib in multiple myeloma)
 - Existing study underway
 - MD PI agreed to prepare an amendment and request additional funding
 - Limited patient population at UW required collaboration with Wisconsin Oncology Network for both studies

ALCAR for CIPN Prevention

- In both cases, although there was MD buy-in, burden fell upon me to:
 - Identify source and formulator of ALCAR
 - Write ovarian protocol (and boilerplate for existing multiple myeloma study)
 - Write R21 for funding (ovarian)
 - Might have been able to get an MD fellow to do that
 - Write and serve as sponsor for ALCAR IND

ALCAR for CIPN Prevention

- Because of tapping into an existing study coordination staff, what I didn't/won't have to do with these 2 Phase II studies:
 - Write budget (but had to provide some details to study staff)
 - Prepare data collection forms
 - Prepare human subjects and HIPAA applications
 - Recruit and consent subjects
 - Obtain study data at each subject's visit

Other Options for Getting Started

- Assist in local research operations by becoming involved in the institution's Investigational Drug Service
- Volunteer to participate in the Pharmacy Committee operations of 1 or more of the Cooperative Oncology Groups

Investigational Drug Services

- IDS required when investigational agents are being utilized in clinical research
 - Ordering and reconciliation
 - Proper storage and return/destruction
 - Standard physician orders
 - Creation/implementation of SOPs for drug preparation and administration
 - Billing and reimbursement

Investigational Drug Services

- Optimal research pharmacist role includes:
 - Review of draft protocol
 - Allowance for comments and modifications
 - Research site control of investigational drug
 - Large centers typically have internal IDS staff and storage
 - Smaller groups, including CCOPs, are more likely to have decentralized IDS services
 - Inclusion in study report authorship
 - Primary or secondary presentation of study results

Cooperative Group Pharmacy Committee

- Protocol review
 - Science
 - Pharmaceutical process and feasibility
- Standardized drug monographs
 - Pharmacology
 - Pharmaceutics
 - Weighting and inclusion of adverse events

Cooperative Group Meetings

- Pharmacy committee
 - Implementation planning
 - Educational planning and reports
 - Distribution of short- and long-term activities
- Disease-oriented committee
 - RPh attendance to identify forthcoming protocols and investigational drug use
 - RPh input regarding practical issues

Cooperative Group Interim Activities

- Drug monograph preparation or review
 - Standardized “boilerplate” for inclusion into every protocol using that agent
 - Includes updates on adverse events
- Protocol review
 - Usually by disease type, occasionally by drug
 - Comments sought on:
 - Science
 - Practicality and implementation

Cooperative Group Pharmacy Committee

- ECOG
 - Chris Fausel, Paul Hutson, Jill Kolesar
- GOG
 - Judith Smith
- COG
- CALGB
- NCCTG
- SWOG

Cooperative Group-Based Clinical Research

- It may even be possible (group-dependent) for a pharmacist to propose and lead a clinical trial
 - E2Z96: Patient-Titrated Methylphenidate for Interferon-Induced Fatigue in Malignant Myeloma
 - GOG: CPC0705 - ALCAR for Prevention of Peripheral Neuropathy

Study Chair or Co-Investigator?

- E2Z96: Study chair
 - Approval by ECOG melanoma DOC and Exec Com, as well as NCI DCPC
 - Funding available through ECOG
 - Placebo and verum tablets made up by the University of Iowa School of Pharmacy
 - No IND was deemed required
 - Study applications and regulatory issues were handled by Central Ops and local ECOG-funded staff

Study Chair or Co-Investigator?

- GOG 1275: Co-Investigator
 - Enthusiastic buy-in from local Gyn/Onc surgeon and departmental collaborators
 - No significant overlap
 - Preliminary supporting data generated by UW scientists
 - Presented to GOG meeting sessions by physician as presumed Study Chair
 - Multiple GOG collaborators identified
 - Biostats, QOL, ovarian

Study Chair or Co-Investigator?

- GOG 1275: Co-Investigator
 - GOG will hold IND (will likely be very similar to mine)
 - Local and national GOG staff will handle the IRB, HIPAA, recruitment, and consenting issues
 - GOG will arrange funding
 - My involvement and recognition in study reports and manuscripts – uncertain

Key Recommendations – 1

- Do a self-assessment
 - Will I get or be able to acquire the time required to take on these research activities?
 - Are my collaborating physicians and study staff on board with my concept?
 - Do we have access to a sufficiently large eligible patient population?
 - Will they be prioritized to other people's studies?
 - “Treatment” vs “nontreatment” (QOL) studies

Key Recommendations – 2

- For what part of the clinical research do I want to be responsible?
- What degree of recognition do I seek for my work?
- Will I be initially satisfied with a supportive role as I gain experience and credibility?
 - How important is “PI” or “Study Chair” to me in the near and in the long term?

Key Recommendations – 3

■ Finally:

- Seek out unanswered questions that interest you
- Seek out collaborators for counsel, mentorship, and integration into “the system”
- Seek out training opportunities appropriate to your immediate and anticipated needs and interests