AMWA MID-AMERICA

Summer 2016

Happy
4th of July!

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A Note from the Editor

Magdalena Berry, MA

Dear Chapter Members,

Greetings!

Welcome to the summer issue! The hollyhocks (or "harleyharcks" as they're known locally) are impressively tall this year, and the tomatoes look good, too…

The deadline for the next newsletter is **Sept. 15, 2016.** Newsletters are generally issued quarterly, at the end of March, June, September, and December.

In addition to our regular contributions, I've included in this issue a reminder about the upcoming **Medical Writing and Communication Conference,** an excellent opportunity to network and enhance your skills provided through your membership in AMWA.

You can find more information about the chapter and some other resources for writers at our chapter web site: www.amwa-midamerica.org

As always, feel free to send any suggestions or contributions!

Magdalena Berry
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Chapter Officers

President: Rona Clair Grunspan, MD
Treasurer: Leslie Neistadt, ELS
Secretary: Linda Landon, PhD
Membership chair: Laura Sheppard, MA
Kansas City events coordinator: Phyllis Edson
Newsletter chair: Magdalena Berry, MA
Webmaster: Lisa M. Balbes, PhD
St. Louis Freelance Luncheon Coordinators: Lisa M. Balbes, PhD, Joanne M. McAndrews, PhD

St. Louis-area Freelance Luncheon Series: TechWrite STL

Joanne McAndrews, PhD
Lisa Balbes, PhD

The TechWrite STL group continues to hold bi-monthly lunch meetings, where a topic of interest to freelance medical and technical writers is presented by a member and discussed by the group, usually over lunch at a local restaurant.

In **March**, Joanne McAndrews and Chris Feely led a discussion about **"Breaking into Regulatory Writing."** This well-attended and lively session covered the types of documents required for regulatory submissions, companies that hire freelancers to write them, and how to get started in this field.

Our **May** meeting covered **"Tips to Make Your Documents and Websites Accessible,"** presented by Alice Fugate. Discussion covered the altruistic and economic reasons to be concerned with accessibility, specific guidelines and tools that can be used to create more accessible documents, and possible future technologies. The visual aids were a big hit – attendees learned how even soup can be inaccessible.

In **July**, Ann Paterson will lead a discussion of both **academic and education-related writing and editing.** How to find freelance opportunities, types of work available, and the expectations of employers in this sector are anticipated subjects.

For the group's 10th anniversary, a **special dinner event** is planned for September 27th at CJ Muggs in Webster Groves, MO. Jay Piccirillo, MD, of Washington University School of Medicine will present "The View from the Top" about journal article submission from the perspective of a current editor-in-chief.

Joanne McAndrews and Lisa Balbes have been co-organizing the group since September 2006, when it was formed as a merger of the local AMWA and STC-CIC groups. A detailed listing of both upcoming luncheons and past topics is available at http://www.amwa-midamerica.org/index.html.

AMWA Mid-America Officers' Meeting Minutes from April 12, 2016

The meeting was called to order at 11:30 pm by chapter president, Rona Claire Grunspan. Seven members were present, including Rona Claire Grunspan, Joanne McAndrews, Lisa Balbes, Laura Sheppard, Magdalena Berry, Linda Landon, and Leslie Neistadt.

Events in St. Louis
The St. Louis TechWriteSTL Freelance group is continuing to organize the St. Louis-area Freelance Luncheon Series every other month to discuss topics of interest to freelance medical/technical writers in the St. Louis, MO area. Speakers on a number of interesting and useful topics present at each meeting. The topic for the May 2016 meeting will be making documents and websites accessible to people with visual impairments. Speakers for upcoming meetings have been arranged. The annual TechWriteSTL dinner will be held on September 27, 2016 to celebrate 10 years of TechWriteSTL luncheons. Joanne McAndrews and Lisa Balbes continue to organize the events. For information on TechWriteSTL activities, please visit http://www.amwa-midamerica.org/.

Events in Kansas City
Phyllis Edson will lead the effort to plan and hold events in Kansas City. Phyllis and Rona Claire Grunspan are planning new events for the Kansas City area members. Contact Rona Claire Grunspan (ronaclaire@gmail.com) if you or someone you know is interested in organizing an event in Kansas City.

Chapter Leader Call with the AMWA Board of Directors
Rona Claire Grunspan and Laura Sheppard have been attending the monthly Chapter Leader Calls and reported on the topics that were discussed. There are 3 upcoming chapter leader teleconferences scheduled for May 9, 2016, Jun 6, 2016 and September 12, 2016 at 11:00 AM EST on each day. Volunteers are sought to attend the calls.
Minutes – The September 2015 minutes were approved.

Signed,
Linda A. Landon, PhD. ELS

SAVE THE DATE!

What: A dinner with AMWA Mid-America chapter members and the TechWrite STL luncheon group

When: Tuesday September 27, 2016, 6:00 to 8:00 pm

Where: CJ Muggs, 100 West Lockwood, Webster Groves, MO 63119

Who: "The View from the Top", presented by Jay Piccirillo, MD, FACS, editor-in-chief of JAMA Otolaryngology—Head and Neck Surgery; Professor, Otolaryngology - Head and Neck Surgery; Vice Chair of Research, Dept. of Otolaryngology; and Director, Clinical Outcomes Research Office, Washington University School of Medicine, St. Louis, MO

Please join us for dinner and a presentation about journal article submission from the perspective of a current editor-in-chief, and mingle with other Mid-America chapter members.

An electronic invitation will be sent to all St. Louis-area AMWA members in July via the Punchbowl website.

Poster: Adapting Pediatric Protocol Designs from Existing Adult Data and Study Templates

Rona Grunspan, MD has offered to share a few posters that she's created for various conferences. I've inserted a .pdf here; you should be able to zoom in on this newsletter so that you can read the poster. I've also attached a .pdf file to the e-mail sent with this newsletter.

Easy as A B C ?

Adapting Pediatric Protocol Designs from Existing Adult Data and Study Templates

Rona Claire Grunspan, MD; Jennifer K. Strickler; Thomas A. Laage, MD, MPH; Emily A. Stube; Charlene G. Sanders, MD

premier research

Abstract

Title: Easy as A-B-C? Adapting Pediatric Protocol Designs from Existing Adult Data and Study Templates

Keywords: Pediatric Clinical Trial, Pediatric Efficacy & Safety Protocols, Pediatric Pharmacokinetic Protocol, Pediatric PK Protocol, Pediatric Protocol Design, Pediatric Study Feasibility, PREA Compliance

Objective: Explain the main differences between pediatric and adult study design that must be addressed. Outline the medical considerations that every pediatric protocol should include. Breakdown protocol elements specific for children and family participation that will permit a study to succeed.

Method: The presentation demonstrates key pediatric considerations for scientific method applied to protocol design to ensure successful and safe enrollment of children. The protocol allows the study design to be acceptable to the referring physician, investigator, the legal guardian, and to the child.

Results: Case studies to be attached to poster.

Conclusion: Concepts in pediatric research design are unique and require special consideration by those first venturing into the realm of conducting clinical research with children as subjects or those facing their first pediatric protocol deliverable.

Background

Performing research studies in children is critical for determining the safety and efficacy of medications in pediatric populations. According to the National Institutes of Health, 70% of the medicines used in pediatric populations have only been tested in adults, leaving a significant need for pediatric studies to provide support with regard to the efficacy, safety, and dosing methods in children. With the permanent extension of the Pediatric Research Equity Act of 2003 (PREA) in July 2012 and similar legislation in the European Union, an increasing number of sponsors are confronted with the task of conducting pediatric studies.

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Methods

- Ensure the protocol and study design are acceptable to the referring physician, investigator, parent/legal guardian, and to the child
- Apply sound scientific methods to ensure successful and safe enrollment of children
- Ensure that preclinical/nonclinical requirements for pediatric studies have been met, including juvenile animal studies
- Identify the differences between pediatric and adult studies
- Specify the medical considerations required for every pediatric protocol
- Include elements that consider of the importance of engaging the family and the child for successful completion
- Ensure that the requirement to inflict minimal harm is paramount and meets investigator, parent/legal guardian, and Institutional Review Board ethical standards
- Address different drug dosing designs to accommodate immature metabolic pathways
- Ensure that age-appropriate and validated pediatric endpoints and assessment tools are employed
- Consider pharmacokinetic (PK) analyses: sparse sampling and application of modeling/simulation to pediatric trials (Traditional PK vs. Population PK)
- Consider any chronic effects of therapy on growth and cognitive development

What are some key differences between pediatric and adult protocol design?

	Pediatric Study	Adult Study
Control	Active comparator	Placebo
Primary Objectives	Safety and tolerability	Safety, efficacy, and tolerability
Age Group(s)	1 day to < 6 months & 6 months to < 2 years	18–65 years
Number of Subjects	N = 52	N = 144
Dose	0.5 mg/kg	40 mg
Pharmacokinetic Analysis	Population-based	Traditional
Dosing Groups	Multiple/complex – dose oldest group first	Single/simple
Standard of Care	Administered prior to study drug	N/A
Postdose Food/Drink Restrictions	None	4 hours postdose
8 Plasma Samples	Each subject gives 4 samples	All time points from all subjects
Pain Assessments	Face, Leg, Activity, Cry and Consolability (FLACC) scale rated by healthcare professional	Numerical rating scale (1–10) rated by subject
Rescue Medication	Mandatory	Available

Objectives

- To meet the medical, ethical, and regulatory requirements for adapting Blue Owl Pharma's medicine that has been developed for adults to the needs and situations of children, in response to an FDA Written Request issued in accordance with PREA
- To use a previously developed clinical trial protocol for adults and adapt it to a pediatric population
- To develop a protocol that will meet the medical, ethical, and regulatory needs for testing of drugs/devices in children
- To assist a company that has not expected this requirement, has no pediatric expertise, and has a deadline to meet; and who has turned to Premier Research for help and is surprised that we simply can't just use their adult protocol

Evaluation

Scenario: Blue Owl Pharma would like to apply a study protocol originally prepared for an adult population to a new study in children.

Problem: Pediatric study protocols require significantly different regulations and subject-specific content.

Considerations: Communication barriers, emotional considerations of parent and child, developmental differences, ethical considerations, practicality and feasibility, and efficacy endpoints.

Conclusions

Concepts in pediatric research design are unique and require special consideration by those first venturing into the realm of conducting clinical research with children as subjects or facing their first pediatric protocol deliverable.

Disclosure

Rona Claire Grunspan, MD: Nothing to disclose; Jennifer K. Strickler: Nothing to disclose; Thomas A. Laage, MD, MPH: Nothing to disclose; Emily A. Stube: Nothing to disclose; Charlene G. Sanders, MD: Nothing to disclose

Results

Case Study – Blue Owl Pharma provided a protocol that they used in a prior adult study. Unaware of the ethical, scientific, and logistical challenges associated with conducting pediatric studies, they want to simply reuse the same protocol, and only revise the study population from adults to children. Blue Owl Pharma was surprised to learn that pediatric studies are not as easy as A-B-C.

Questions to consider when writing a pediatric protocol compared with an adult trial are listed below:

Overall Study Objective	Is the overall objective of the study still relevant for pediatric patients? Will this age group benefit from the study drug? Will there be investigator interest for this particular study?
Therapy	What therapy are we using? Is there a comparator to the study drug? Did the adult study have a placebo? Is the standard of care different for children? Is the medical condition for which the adult drug was approved, etiologically, biologically, or physiologically, the same in children? Are we dealing with off-label use? Will exposure to therapy mandate long-term follow-up for monitoring developmental and growth outcomes?
Dosing	▪ Significant differences in body sizes (not only in comparison with adults but also among children of various ages) are confounded by physiological differences and maturational changes ▪ Congenital defects and developmental issues are often of greater concern in pediatric populations ▪ How will the drug be administered? Will a parent need to administer it at home? If so, is it child-friendly? How often? Are pediatric formulations needed? ▪ Physiologic factors suggest that this age-cut-off may still represent a transition stage with respect to the various ADME processes ▪ Differences in "binding" constituents ▪ Physiologic – pharmacodynamic differences are less precise: coagulation cascade ▪ Vascular resistance ▪ Tumor tortuosity ▪ Age-dependent genetic differences
Duration and Logistics	How long will the study last? How many visits to the study site will be required? Will the visits be kid- and family-friendly? How much time will it take from their regular life activities? How much school will be missed? Not only the child but the entire family is involved.
Inclusion/ Exclusion (I/E) Criteria	▪ Narrow inclusion/exclusion criteria further decreases the limited number of eligible patients. ▪ I/E criteria are often different than for adults. ▪ Concomitant therapies and medications are often different ▪ I/E criteria must be adjusted for age-specific subgroups.
Age Groups	Many age subsets require studies, because not just one study can cover all of the pediatric population. Birth through adolescence spans a wide range of organ developmental maturation (eg, CNS, liver, kidney, lung, skeletal, reproductive, and immune systems), which may affect drug pharmacokinetics, efficacy, and safety. Age groups to consider: ▪ Preterm: Gestational age < 37 weeks ▪ Term: Gestational age 37–42 weeks ▪ Postterm: Gestational age > 42 weeks ▪ Neonate/Newborn: Birth to 28 days ▪ Infant: Birth to 1 year ▪ Young, Immobile: Birth to 6 months ▪ Older, Mobile: 6 to 12 months ▪ Young Child: 1–5 years ▪ Toddler: 1–3 years ▪ Pre-Schooler: 3–6 years ▪ School Age or Older Child: 6–12 years ▪ Pre-Adolescent: 10–12 years ▪ Adolescent: 13 to 18/21 years
Sample Size	▪ Small sample size/sparse data effects are demonstration of statistical significance ▪ Wide variance of patient data sample sizes across age subcategories ▪ Each patient may not be able to supply more than a few data points ▪ A patient may not be able to complete entire study but still has usable data ▪ May need to consider adaptive design ▪ May need to consider Pharmacometric Modeling and Simulation ▪ May need to consider Population PK analyses or non-compartmental PK paradigms
Regulations	In general, new products are developed for use in adult and pediatric patients. Pediatric product development should be integrated into the adult development program and not be an add-on or afterthought, and must meet pediatric regulatory requirements. ▪ Requires pediatric-focused post-marketing safety reporting for all products studied under BPCA or PREA ▪ Requires tools for this integration including those provided by the pediatric legislation: BPCA and PREA ▪ Must be conducted with the same scientific and ethical rigor as for adults, with additional ethical protections for children (Subpart D 21CFR 50.50-50.56)
Ethical Issues	▪ Healthy adults can volunteer for a study; children cannot ▪ Children cannot consent to participation – both parental permission and the child's assent often are required ▪ Moral imperatives: Children's vulnerability must be protected. Added stress, burden, or guilt, no matter how inadvertent, conflict with social norms and child advocacy
Other Considerations	▪ Special pediatric-focused facilities, equipment, nurses, laboratories, and expertise are needed ▪ Limited patient population because children tend to be healthy ▪ Children's illnesses tend to be acute, so a chronic patient population may be limited ▪ Small populations may lead to multicenter, and often international, studies to enroll an adequate number of patients ▪ Pediatric scales or assessment tools may need to be designed and validated prior to use when none exist