

# CARA

THERAPEUTICS

Josef Schoell  
Chief Financial Officer  
Cara Therapeutics  
1 Parrott Drive  
Shelton, CT06484  
August 21, 2008

Br. 2

Licensing Assistant Section  
Nuclear Materials Safety Branch  
US Nuclear Regulatory Commission, Region I  
475 Allendale Road  
King of Prussia, PA 19406-1415

06-31254-01  
03037490

RE: Change in Radiation Safety Officer

I am writing to inform you that our current Radiation Safety Officer, Conrad Cowan, will be leaving Cara Therapeutics as of September 1, 2008. We would like to have William Martin take on the responsibilities of this position. Dr. Martin's resume and summary of his experience with radioactivity is enclosed.

Please amend our license, 06-31254-01, to show that Dr. Martin is now the Radiation Safety Officer. If you have any questions or require additional information feel free to contact Dr. Martin at 203-567-1539.

Sincerely



Josef Schoell

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REGION I  
2008 AUG 26 AM 10:20

142739  
NMSS/RGNI MATER. ALS-002

**William H. Martin, Ph.D.**

[wmartin@caratherapeutics.com](mailto:wmartin@caratherapeutics.com) or [wmartin0@snet.net](mailto:wmartin0@snet.net)

**SUMMARY OF QUALIFICATIONS**

- Sixteen years of experience managing technically complex R&D programs and operations
- Skilled at developing and applying biochemical and cell biological assays for high throughput screening, SAR as well as for Safety issues
- Strong record of success managing teams up to 40 people with contributions essential to 11 developmental candidates and 12 patents
- Considerable experience leading cross-discipline/line projects to implement new processes and software.

**PROFESSIONAL EXPERIENCE**

**2007 – Present: Director at Cara Therapeutics** of group responsible for:

- Target selection
- Biochemical and Cell Biology assay development
- HTS and SAR studies
- Compound characterization in secondary and kinetic assays

**2005 – 2007: Director at Pfizer** of groups responsible for:

- SAR development for hit follow-up libraries and medicinal chemistry
- Cytometry Core with FACS and Cell Imaging capabilities
- Safety screens for early Drug Discovery projects including an *in vitro* micronucleus assay, Dofetilide binding and numerous whole cell imaging assays
- Assay development for high throughput screens (HTS)
- Validation and characterization of HTS hits, including SAR follow-up and kinetic characterization of compounds
- Head of the global Plate Based Pharmacology Initiative responsible for implementation of biochemical data analysis software at all of the Pfizer research sites
- Modeling Discovery processes using Agile and Lean approaches

**1999 – 2005: Manager/Associate Director/Director at Pfizer** of groups responsible for:

- Development of HTS assays, validation and characterization of HTS hits, SAR and secondary assays. Supplied lead matter for 1/3 of the site's clinical candidates.
- HTS > 35 million compounds and 25 projects/year
- Developing safety screens for early Drug Discovery projects including an *in vitro* micronucleus assay, Dofetilide binding and numerous whole cell imaging assays
- Groton site representative for the multimillion dollar and multiyear Evotec OAI collaboration to implement ultra HTS equipment cross sites
- FACS facility collaborating with Reagent Provision Group, ADME, Safety Sciences as well as all of the Therapeutic Areas
- Groton Business lead to the Evotec Collaboration

- Business lead for Biology data analysis software for IC50 calculations and HTS data analysis

**1992 – 1999: Laboratory Supervisor at Pfizer** of group of four associates responsible for:

- Development and implementation of over 50 HTS
- Validation and characterization of hits from all of these programs, in some cases continuing to run SAR and kinetic characterization studies well into the program's development
- Identifying novel lead matter that led to 11 Developmental Candidates
- Contribution to 13 publications and 10 patents

## **EDUCATION**

**1984 Ph.D. Pharmacology**  
 Medical College of Ohio  
 Toledo, Ohio

**1992 M.S. Biomedical Engineering**  
 The University of Connecticut  
 Storrs, Connecticut

**1980 M.S. Biology**  
 The University of Miami  
 Coral Gables, Florida

**1977 B.A. Biology**  
 The Johns Hopkins University  
 Baltimore, Maryland

## **RESEARCH EXPERIENCE**

**2007 –:** Cara Therapeutics  
 Target selection  
 Assay development  
 High throughput screening  
 Structure activity relationships  
 Compound characterization

**1992 – 2007:** Pfizer, Inc  
 Assay development  
 High throughput screening  
 Structure activity relationships  
 Compound characterization

- 1989 – 1992:** University of Connecticut  
Biomedical Engineering  
Digital imaging processing of scanning electron micrographs
- 1987 – 1989:** Yale University  
Department of Cellular and Molecular Physiology  
Ion flux in red cells
- 1985 –1987:** University of Virginia  
Department of Pharmacology  
Subcellular mechanisms that underlie the release of hormones and neurotransmitters by exocytosis.

#### **AWARDS**

- 1987-1989** Cystic Fibrosis Foundation  
Postdoctoral Fellowship
- 1986-1987** National Research Service  
Postdoctoral Fellowship
- 1980-1984** Predoctoral Fellowship  
Medical College of Ohio

Patents and publications on request

<b>Cara Therapeutics</b>	<b>RADIOACTIVITY TRAINING AND EXPERIENCE</b>
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Date: August 20, 2008

Name: William Martin

Title: Director

Department: Molecular Screening

Education:

B.A. 1977 Johns Hopkins University

Ph.D. , 1984 – Medical College of Ohio

### TRAINING AND EXPERIENCE

Type of Training	Where Trained	Duration of Training	On the Job (Yes/No)	Formal Courses (Yes/No)
a. Radioisotope Methodology Class covered isotope properties, calculations and measurement as well as handling techniques and spill clean up	Medical College of Ohio	4 credit hours	No	Yes
b. Radiation Training	University of Virginia	4 hours	Yes	Yes
	Yale University	4 hours	Yes	Yes
	Pfizer, Inc.	18 hours	Yes	Yes

### LABORATORY EXPERIENCE WITH RADIOCHEMICALS

Isotope	Maximum Amount	Where Experience was Gained	Duration of Experience	Type of Use
14C	250 uCi	Medical College of Ohio	2 years	Research
32P	1 mCi	University of Virginia	2 years	Research
32P	1 mCi	Yale University	2 years	Research
86Rb	10 mCi	Yale University	2 years	R&D
125I	10 mCi	Pfizer, Inc.	2 years	R&D
33P	1 mCi	Pfizer, Inc.	7 years	R&D

## **Radiation training at Pfizer**

### **Introduction to Radiation Safety (1<sup>st</sup> Required Class, 2 hours)**

#### Topics Covered:

Radiochemical Manual	Contact Numbers
NRC Form-3	Radiochemical Tracking System (RTS)
Laboratory Responsibilities	Laboratory Safety Practices
Procedure to Begin Operation	Swipe Test Procedures
Ordering Radiochemicals	Low-Level Radioactive Waste
Emergency Procedures	Dosimetry
Bioassay Program	ALARA Policy (exposure minimization)
Exposure History	Training and Experience Records
Isotope Data	Regulatory Documents
Radiochemical Supervisors	Laboratory Registration

### **Radiation Safety Training**

**Audience:** All new radiochemical users that have attended the “Introduction to Radiation Safety” class.

**Description:** ½ day seminar

#### Topics Covered:

##### Introduction

- What is Radiation?
- Types of Radiation (atomic structure)
- Shielding
- Units of Activity and Dose
- Decay (Half-Life)
- Dosimetry

##### Background Radiation

- External Exposure
- Internal Exposure

##### Laboratory Issues

- NRC (Nuclear Regulatory Commission)
- Sealed Sources
- Laboratory Procedures
- Postings

Emergency Procedures  
Time, Distance, Shielding  
PPE  
Survey Meters  
ALARA (As Low As Reasonably Achievable)

Biological Effects  
Acute vs. Chronic  
Whole vs. Partial  
Radiation Effects  
Cancer

Radioactive Waste  
Types of Waste  
Solid  
Aqueous Liquid  
Biological  
Sharps  
Scintillation Fluid  
Mixed Waste  
Waste Collection

Q & A

### **Annual Radiation Safety Training**

Audience: All employees who use radiochemicals and their supervisors.

Frequency: This annual refresher course is held each November.

Topics Covered:

Regulations

NRC (Nuclear Regulatory Commission)  
Rules and Regulations (Parts 19 and 20)

Laboratory Issues

Laboratory Procedures  
Sealed Sources  
Personal Protective Equipment (PPE)  
Emergency Procedures  
Time, Distance, Shielding  
ALARA (As Low As Reasonably Achievable)

Annual Reminders

**Review of any issues**

**Current Topic**

**Discussion of any current subject pertaining to radiation and radiation safety**

**Q & A**



This is to acknowledge the receipt of your letter/application dated

8/21/08, and to inform you that the initial processing which includes an administrative review has been performed.

Amendment (06-31254-01) There were no administrative omissions. Your application was assigned to a technical reviewer. Please note that the technical review may identify additional omissions or require additional information.

Please provide to this office within 30 days of your receipt of this card

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A copy of your action has been forwarded to our License Fee & Accounts Receivable Branch, who will contact you separately if there is a fee issue involved.

Your action has been assigned **Mail Control Number** 142738.  
When calling to inquire about this action, please refer to this control number.  
You may call us on (610) 337-5398, or 337-5260.