

Trading Goessman Lab Desk for a Cube Farm

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PhD (Chemistry) 2004 Kaltashov Group



Introduction

- I have been coming to UMASS for the last 10 years to talk about alternate/non-traditional careers in science – and I have always been happy and honored to do so
- This presentation is essentially my journey as a UMASS student to how I ended up doing what I do now, what I learned, what I wished I had known earlier
- Hope its helpful to the current students as they navigate their career

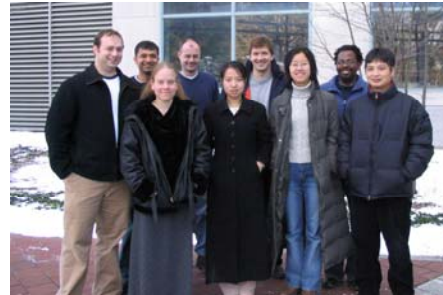
Caveat – this is my story and its opinionated and likely biased; not everything will apply to you all – we are after all individuals

Outline of my Talk:

- What I do now
- How I got here
- Some advice on what I wish I had known

About Me

- A big part of my life has been spend here in Amherst
- PhD in (Analytical) Chemistry with Igor Kaltashov
- Also a product of UMASS Amherst Undergraduate
- Current: Director (Head) of Regulatory Affairs CMC at Blueprint Medicines
 - Blueprint Medicines – Discovers and Develops drug for Unmet Medical Needs (Rare diseases, especially oncology)



Lets start with what I do now...

What I do now – Regulatory Affairs CMC

What is Regulatory Affairs in the Pharmaceuticals (Biotech) Industry?



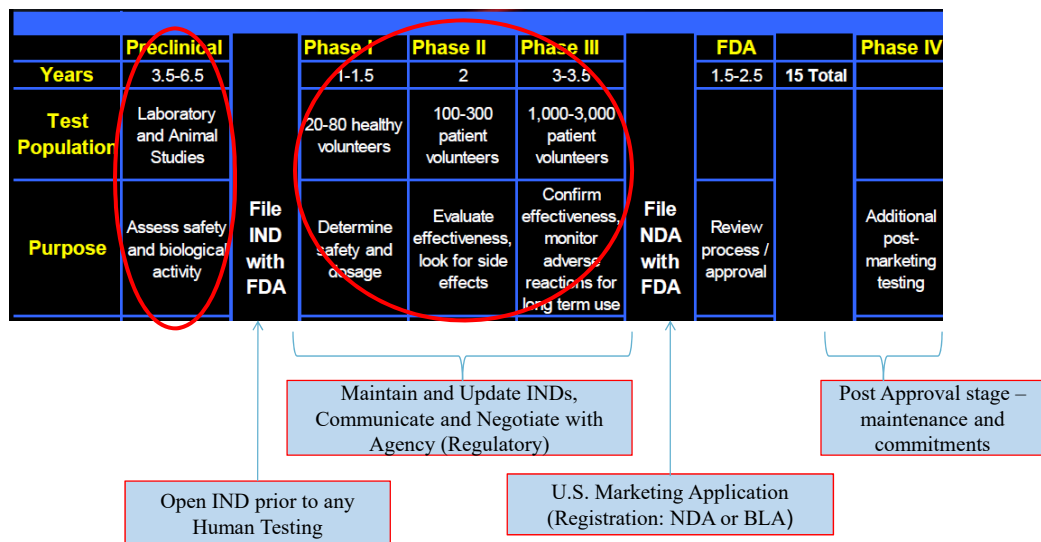
This role along with countless others that I didn't know even existed as a career option...

Glorified admins? Project Managers?

Regulatory affairs typically refers to that group of scientists who formulate the strategy for interacting with the regulatory authorities in various countries as well as the tactics of securing responses to questions dealing with submissions and maintaining communication post registration. Many of the scientists who populate regulatory affairs groups were originally involved in drug discovery or development. They need to understand the processes involved in drug discovery and development to accurately represent the science to the regulatory authorities. They are also involved in the compilation of the information in the form of investigational new drug submissions or new drug applications for final registration. With the evolving landscape of regulatory guidances, they also need to remain state-of-the-art in what the regulatory agencies are thinking and saying. <https://www.sciencedirect.com/topics/medicine-and-dentistry/regulatory-affairs>)

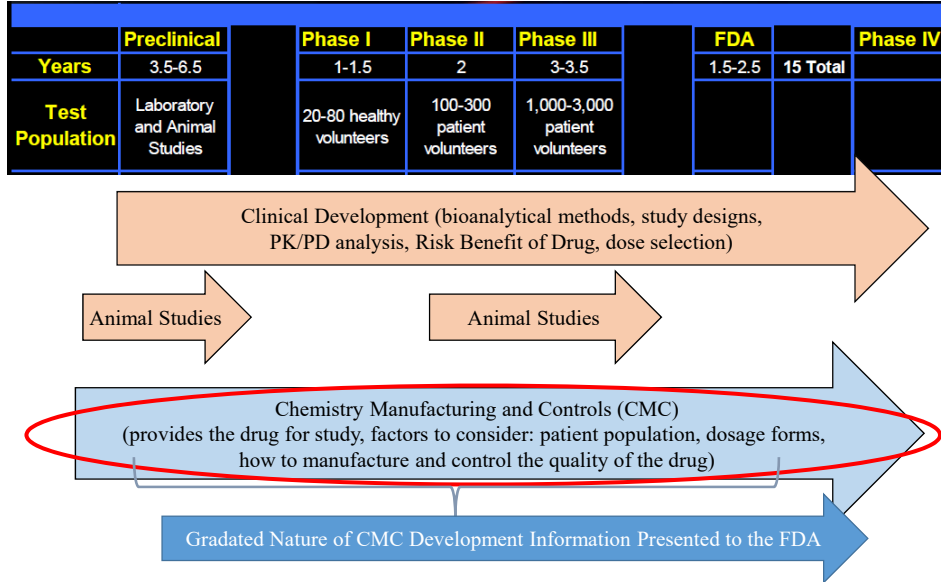
To understand my role, lets start with an overview of drug development

General Drug Development Process in the United States

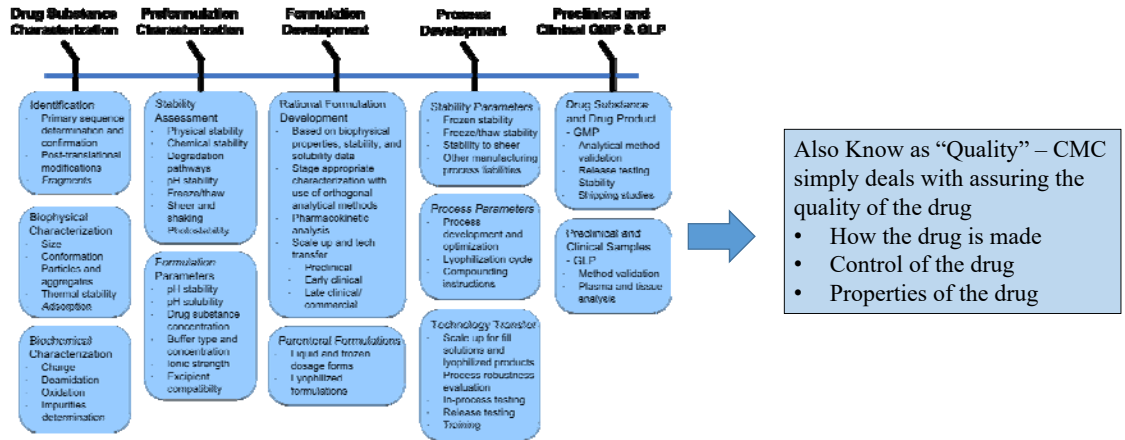


Drug Development Process - ISPE

Three Major Streams of Drug Development

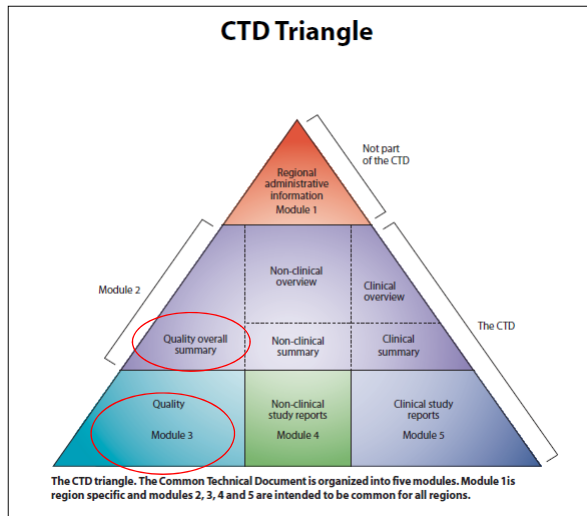


Sheer Depth of CMC activities



All the information has to be properly presented to the FDA, in a phase appropriate fashion...called dossier development

Dossier Development: A Big Part of Regulatory Affairs



ICH.org

Module 3: all about your molecule (sufficient detail)

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http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R1_Quality/M4Q_R1_.pdf

Dossier Development during investigation: preventing clinical hold

- Initial IND: Safety assessment (30d review by FDA)
- Amend IND with CMC changes (new process, formulations, stability, better methods etc.)
 - Each country will have a different expectation
 - E.g. FDA not concerned with shelf life but EMA and Canada is!
 - Major changes occur as development progresses, expected to notify agencies of changes
- CMC amendment (CFR) should be once every 60d.
 - Balancing when to submit
 - Balancing too much information v. to too little (phase dependent)
 - Giving development flexibility v. questions for agency

Next Drug Development is a Global Activity...

Drug Development is Global



This was just a CMC view – same goes for Clinical – Patient populations from all over the world supports a marketing application

Fun and Challenges

- **FUN:**
 - *Keep up to date with ever changing regulatory landscape*
 - *Not all agency expectations are in guidance documents! Evolving- requires you to think and analyze – there is no “textbook answer”*
 - *Learn the fundamentals of different field (microbiology, cell culture, aseptic processing, pharmaceutical processing, bioprocessing)*
 - *Solving problems within the grey zone and applied problem solving*
 - *Working with people from various disciplines – learning constantly*

Challenges:

- *Working with people from various disciplines*
 - *Development activities prioritization: Must have v. good to have v. “ooh that’s interesting”*
 - *“it was good enough in school” or “this is too much rough estimation in school...”*
 - *“What is the answer?” Very fact specific case by case analysis.*
 - *We should do XYZ because AB at conference M had a poster*
 - *I read XYZ and I Know ABC lets make this and that to improve (no reason)- \$\$\$ later no improvement , competitor comes up with a worse drug but hits the market first (idea was based on conjecture than sound science – person know it all in wrong discipline)*
- *Contract Manufacturers*
- *Dependent on people to provide you the information (you are managing a project without power over your team)*

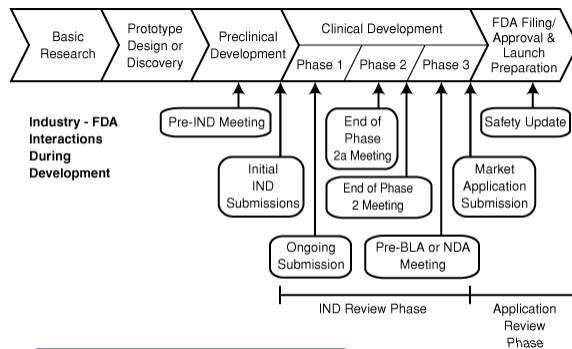
Working with Timelines

Agency Meetings: B v. C

When to begin process Validation? BLA v. NDA

How much stability data acceptable?
Data extrapolation?
Drugs v. Biologics

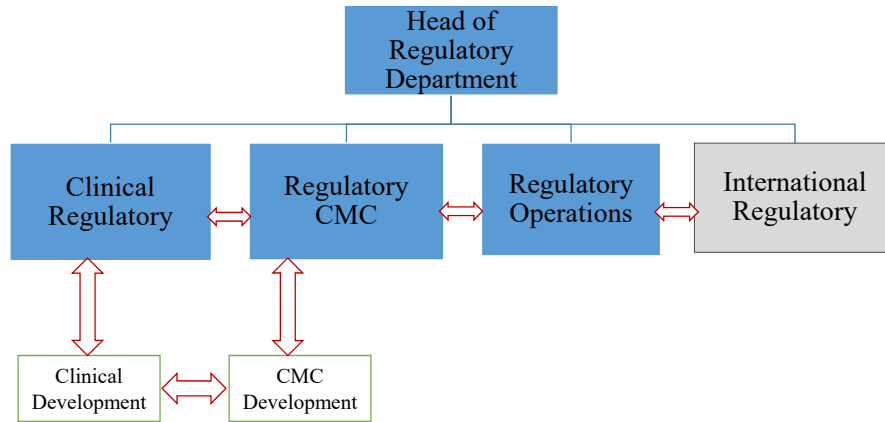
Turnaround agency question:
Canada: 48 hours
Germany: 15 days
FDA: depends on the question



Timing of Submission among various countries

<http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm077262.htm>

Department of Regulatory Affairs



Regulatory CMC is unique – must be technically savvy to talk with internal scientific experts and with FDA experts

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Did I always know I wanted to go into Industry?
How did I end up doing what I do?



Best to start with how I got into the industry

Undergraduate Years

- 1998 – chemistry major -- floating along
- Parents want me to study medicine but boy do I dislike interacting with people (introvert)!
- I have horrible “bedside manner,” impatient, blunt and easily irritated
- Plus I have a strong dislike of anatomy and physiology
- Chemistry, Math and Physical Sciences – I could just float without making any effort
- Summer of 1998 comes along – Professor Uden - sets me up with an Internship at Pfizer (Analytical Labs)with an UMASS Alumni
- I loved it! Hey! Working in industry is something I could do for a living!



Pfizer

- At the end of my internship – I talked with my mentor - Bryant Nelson – I wanted to work in the industry
- His answer
 - Sure – but - go get your PhD unless you want to hit a glass ceiling in Analytical Chemistry
 - UMASS Grad School? Frowned upon to attend the same undergrad and grad school
 - Why did you join Umass? – “I didn’t choose Umass I chose Prof. Uden”

Prof Uden – was a well renowned Analytical Chemist with great Industrial Contact.

Learned the value of Alumni connection and I knew then I want to join the industry

But the other underlying reason – I knew I was an average scientist, great in an applied environment of the industry – but I could not survive in the academia.

Graduate School

- I joined UMASS anyway and selected Prof. Uden as my advisor (Analytical Chemistry)
- I just loved Western Massachusetts and I loved being in UMASS – I knew I was going to get a good education – and to me it was about potential industrial contacts and jobs after graduation.
- Overall I did 3 stints at Pfizer – last one was end of first year of graduate school (eye-opener)
 - Noticed contraction of Pharmaceutical Industries (Pfizer mergers with Warner Lambert, Pharmacia)
 - Outsourcing was beginning
 - And I panicked...



Second Year of Graduate School

- Prof. Julian Tyson – “hardest part is getting your foot in the door...”
- Decided to go beyond analytical separations and try something more cutting edge – proteomics and mass spectrometry
- Joined Igor’s group (Analytical Chemistry)
 - He was upfront and made his expectations clear
 - Tight knit and close group
- To be a more viable candidate in the future (and also cast a wider job net) – I started taking Chemical Engineering classes on the side – BS ChE 2003.

Why did I choose analytical?

Simply put – certain element of luck – and being a paranoid future looking person – that’s where the most significant industrial jobs are – I started looking at the job market back in school and to this day I monitor the trend

First Job: Schering-Plough

- Joined in Oct 2004 –first job - Right place right time...
- Handed the Analytical Development lead for Vorapaxar
- Key drug for Schering Plough

Hands on CMC Drug Development, Dossier Development and Regulatory Knowledge

- Tribal Knowledge in large historic organization
- Started considering moving out of laboratory roles for personal growth
 - Enjoyed regulatory writing and crafting responses to regulatory agencies

Law School and Regulatory Affairs

- 2009 – wanted out of New Jersey and wanted out of laboratory based position
- Landed a job in Vertex in the Analytical Department in 2009
- Applied to Law School (PT) and Admitted (wanted to do Patent Law)
- While in Law School - a year later moved to Regulatory Affairs CMC (lateral)
 - Sold my abilities to the hiring manager

Why didn't I quit law school after I got into Regulatory?

- Law school teaches you how to think and write – craft an argument to suit your position – persuasive writing
- Immensely helpful in regulatory writing



IMMUNOGEN Regulatory CMC Biologics

- 2012 – Joined Immunogen – Regulatory CMC in Biologics
 - Different than small molecule – more opportunity than small molecules (thinking about future opportunities)
 - Interview with the head of Regulatory and Head of Bioassay
 - PhD and my breadth of knowledge (chemistry, biology, proteins, engineering principles)
- This is where I found my “voice”
- Loved the Small company environment



- 2016 – Joined Alexion – Post Approval Regulatory Affairs
 - Layoffs in early 2017
- Joined Blueprint Medicines Immediately Afterwards
 - Networked via my then Alexion Supervisor
 - Tough decision – leave biologics but opportunity to build and head a department



- Best Decision Ever!
- Small company – jump in take control of the regulatory CMC strategy
- Build report with the existing CMC development scientist
- Not a single boring day!
- First Challenge:
 - What do we do - we cannot meet FDA's expectations per the guidance...(working in grey area)"

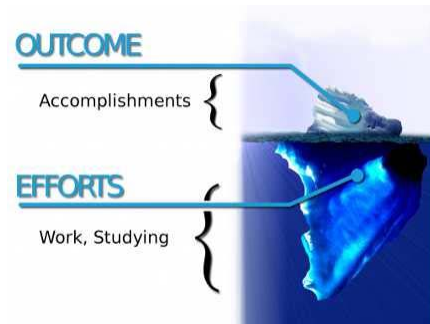
Working within Grey Areas

- Balancing Risk – Interesting Problems to Solve
- There is no right or wrong answer most of the time
- Use good scientific justification along with the principles of FDA views
 - Registration Batch Sizes (engineering principles)
 - Comparator Sourcing from European Union (crafted argument based on legal persuasive writing)
 - An unconventional manufacturing approach (good science)



What I wished someone had told me early on in my career...and some final comments

I have had some luck based on decisions I have made ... but also my fair share of lessons learned



The Art of Public Speaking

- Both UMASS and Igor gave me opportunities to speak/present in public forum- presenting to wide audience
- Do not take this opportunity lightly – learn from your mistakes – extremely important in industrial setting
- I learned from Igor:
 - (1) He preparations for presentation, animations and the art of “simple delivery of the message”
 - (2) His statement that “you should not always trust everything you read in articles”
 - (3) His hard work, ethics and scientific problems solving skill set – showed me I wasn’t cut out for Academia!

Memory Lane of my Public Speaking Debacle: UMASS Journal Club, Delaware Mass Spectrometry Society, First few Presentations in Industry

Job Interviews – Differentiate yourself

Public speaking brings confidence and it will help with you job interview
Every PhD or (as you climb the ladder) YOU will present routinely and even as part of job interviews

- My first interview – Proctor and Gamble
 - Went in with big ego - “...*doesn't drive his work to completion*”
- Interview with Schering Plough (2003 and 2004)
 - I differentiated myself, less egotistical approach

- You get better at the interviews with time
- My first supervisor told me to make sure I interview at least once a year and I do
- This is your opportunity to sell yourself
 - Believe it or not this Introvert loves talking about himself

Writing

Learn to write – do not take this lightly

- Take advantage of what UMASS has to offer
- Not just technical writing but also soft writing skills
- Good grammar is important, but concise well constructed sentences makes the difference
- Vast amount of written communication in real world (email, memos, reports)
- Find your style
- Think about your audience

Writing in a Regulatory Environment is very different that scientific writing

- To the point and brief
- Scientific principles within the framework of regulations and guidance

What helped me with the writing was Law School...especially persuasive writing

Network, Network, Network

- Alumni (school as a whole has this shortcoming), but its changing
- Only way you will know what's out there and how to get there...there is a wide world of opportunity beyond traditional science based career
- You will be measured against big names...get your foot in the door and impress

Linked has been very helpful in this area to me (and I am an introvert)



Soft Skills – Know Yourself

- Know yourself – short comings and what you like/dislike
 - Soft Skills are very important
 - Have a sense of humor
 - Separate the problem from the people – don't argue for the sake of arguing
 - Walk away and come and fight another day
 - Blunt and an Introvert – it's a bad mix – but people change
 - Like big picture and continued learning and practical applied problem solving
 - Constantly learning new areas (PK, PD, Toxicology, Clinical Development)



One of the Biggest Key to Success: a Good Supporting Boss

- This applies everywhere
- Take a tough but an honest supportive boss
- I have had my shares of bosses but I have generally been lucky

“A bad job with a Good Boss is Better than a Good Job with a bad boss”

There’s a difference between a boss and a leader. The boss usually gives orders and is a “know it all” kind of person. A true leader ignites a spark in you to do more and become more. They’re willing to always learn and listen.

UMASS is a wonderful school

- Enjoy it – my time here is what I most fondly remember
- Its up to you to take advantage and learn

- Don’t feel entitled – just because you have a PhD (trust me – you know nothing of the “real world”
- Set your goals - Never was the one to view “all things will work out” or “it will happen if its meant to be
- Have backup plans

