# Hi Reddit! I am Joseph Glajch, the Director of Analytical Development for Momenta Pharmaceuticals. Ask me anything about biosimilars or what it's like for chemists to work in the private sector.

AmerChemSocietyAMA [1] and r/Science AMAs[1]

[1]Affiliation not available

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the WINNOWER

REDDIT

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Hi there! I have a couple of questions.

- **Could you talk a little bit about what is involved in development of a biosimilar, related to the original product?** Meaning (at the risk of oversimplifying), developing Copaxone requires the idea of how the drug works to treat MS--understanding the disease state on a molecular level and conception of how to design a molecule to treat that disease. Then develop the molecule, test, adjust, test again, etc. But with a biosim, you already have the end product in mind, right? So how does the development and design begin? I realize that the process is more complex than simply reverse-engineering the original molecule, but could you explain a bit about how the design is approached?
- **Also, is the goal of biosim development to optimize disease treatment, or to mimic the original drug as closely as possible?** If, during the development of Glatopa, it was discovered that a slightly different structure of the molecule resulted in better treatment outcomes, would the team pursue the better outcomes, or the product most closely resembling Copaxone?

Thanks for your time and attention!

Ask_Your_Mother_

Good questions. Copaxone and Glatopa are not biologics or biosimilars, but I can try to answer the questions in the realm of biologics. You are correct that the development of a new drug or biologics requires understand what works and perhaps how it does. A biosimilar just needs to show that it is highly similar (FDA term) to the original and relies on the clinical and commercial experience of the first drug. This is why for biosimilars (and generics before them) the package insert and instructions are identical. If someone were to develop a somewhat better version, it would be a new drug (or have some referred to it, a biobetter), but this would need a more fully developed package for approval.

This may seem like a silly question, but how much actual "science" does an average chemist do in a day in the private sector? A lot of people I know with science or engineering degrees end up in

positions where they very rarely actually perform any experiments or do any work that even resembles their degree, and I'm worried that I'll end up in a boring position like that if I don't stay in academia once I finish my PhD.

camtaro

A good question about actual "science" done. While it may be true that many of us spend less time in the lab than we used to in graduate school, the main aspect of a science-based education is to teach us how to think and solve problems, despite setbacks and "failures." In that respect, we are using our science education all day in various aspects of what we do.

How similar are biosimilars? How likely are they to cause reactions etc that differ from their reference products and how worried should we be as pharmacists when patients switch to a biosimilar product?

We recently went through all of this in the UK with infliximab over the last couple of years, and it's been pointed out to me many times that Remicaide (the original infliximab brand) have altered their product over 30 times since it was licensed. Therefore (the argument goes) it's effectively a biosimilar of itself and so we probably needn't be worried when switching patients to 'official' biosimilars since we didn't particularly care (or even know) when Remicaide changed it's product.

Would be interested to hear your view on this transition though, from the point of view of the underlying chemistry.

(also thanks for doing the AMA!)

_Leigham_

The hope is that biosimilars are as similar to the original biologic as different batches of the biologic are to itself. Those of us in development and approval are trying to make this happen.

Hi Dr. Glajch, Couple questions;

(1) Why did you choose to go into the private sector rather than take the academic route?

(2) If you could go back to the earlier days of your career, what mistakes, if any, would you try to avoid or fix?

(3) Do you have any personal advice for younger chemists attempting to adapt to the trends of the industry which may emerge in the future? Is it generally better to stay flexible/interdisciplinary or pick a focus and stick with it?

Thank you for taking the time to do this. As an undergrad, AMA's like these provide invaluable advice.

TheBlackLagooner

Good questions. I spoke to some of these in other responses, but I will expand a bit here. I chose the private sector because in my field of Analytical Chemistry there were many challenging problems that I could work on. As for mistakes, can't think of too many – one thing that I did try to do was be flexible and work on somethings with other groups not related to my primary work to expand my horizons and experience.

Did graduating from such a prestigious university, such as Cornell, place you ahead of other competition, say, someone graduating from a basic level state university under the same degree?

Would graduating from said state university, hinder one's ability to move forward quickly in their career choice?

Please be frank.

MisfitToSociety

Good question regarding schools. I don't think any particular college is necessarily the most important in moving forward with a career. I had many colleagues in grad school who were successful that came from both private and state schools, small and large, etc. It is really up to the individual to take advantage of what a particular school offers.

Hi there,

PhD candidate in chemistry defending about 7-9 months out .

Do you ever miss bench work or method development for hplc? I assume you have done a decent amount of getting your hands wet in lab and more leadership/direction and big picture work. I get sick of just working on my computer (papers,presentations, etc) and talking to people all day, and I like getting into lab.

pegleg364

I can relate to your desire to get into the lab and it is one of the things I miss in my current job (as an aside, I have taking up a lot of cooking at home to make up for this!). But I also know that I can be more effective in an overall role by working with others both in my area and others and this provides plenty of challenges for my work.

What is the likelihood that the reforms to the Affordable Care Act will negatively impact the private pharma sector, in regards to the (dis)continued approval of chemical research? Could this be offset (in terms of profitability) by a potential increase in private insurance holders?

-Sorry if these questions don't make sense, I am not a US citizen so am unclear on how it all works!

HerbziKal

I think the ACA and its pathway for biosimilar will actually be a positive for new research and drugs in the same way that the generic drug pathway worked starting in the 1980s. Companies with drugs that are going off patent or that will be replaced by generics or biosimilars have even more incentive to develop new drugs or therapies.

I am prescribed a fairly expensive biologic, Humira, which is still under patent. Could biosimilars be used to create a cheaper generic version before patent protection expires?

This is also the first time I have ever heard of biosimilars. Would it be expected that a biosimilar would have different and maybe less severe side effects that the biologic version has(in Humira's case cancer risks)?

pyman

Good to hear from people using medicines like biologics. In fact, a main hope for bioimilars is that they will be more affordable in the same way that generic small molecule drugs have reduced the cost and expanded access in the past. Biosimilars will still need to wait for patent or exclusivity periods before

they are marketed, but the hope is that they will have a major positive impact on health care.

What are some of the challenges that are unique to working with biosimilars (as opposed to traditional small-molecule drugs)?

halbob

Good question. Biosimilars are larger molecules and are also not one unique material, but rather a population of related substances with different levels of modifications and glycosylation, for example. So it is more challenging to compare a population of materials to another rather than just one single molecule to a copy of that molecule.

Hello Joseph, thanks for taking time to do this AMA!

Couple of questions:

1. What are some major differences in cost structures between developing biosimilars vs. biologics vs. small-molecule drugs?
2. How was it like to transition from doing work in the lab/plant to being in a more managerial/administrative role? Why did you make this transition?

edwinksl

Good questions. As for 1. the major difference is the level to which one needs to characterize and then develop a process to make a biosimilar vs. a small molecule. It is at least 1-2 orders of magnitude more time and $$ to do this. As for 2., I made the transition partly because I could be more effective overall and have more influence with a group than doing work just on my own.

Thank you for doing this, Dr Glajch. Are there current examples of successful biosimilars? And what does the process of creating a new biosimilar look like in terms of time and effort?

SourKrautCupcake

Good multi-tiered question. Biosimilars have been available in Europe for more than 10 years. In the US, as part of the Affordable Care Act of 2010, biosimilars were granted a pathway for approval through the FDA. So far four biosimilars have been approved in the US but many more are under development. The development and approval process generally takes 4-7 years which is shorter than a new drug since the clinical trials are more limited. Most of these are in the early stages of product launch or preparing for launch; so the regulatory process was successful but the commercial success remains to be seen.

I've noticed for glycosylation analysis that there are a lot of methods used in academia that don't seem so popular in industry (like, they aren't used at all in industry). Can you comment on this? Are there any methods you/your team has tried and concluded; "this just doesn't work".

real_eparker

Good question regarding academic vs. industrial use of techniques. While I cannot comment on any specific technique, often in industry the question we are trying to solve is a bit different than in academics. As an example, in the development of biosimilars (or even more traditional generic drugs),

the question is often – how similar or equivalent are these and not what the actual structures are. Hope that helps a bit.

Dr. Glacjh,

First, I would like to say thank you for doing this AMA! I have a quick question for you: I am currently an undergraduate working in statistics, with plans to pursue a graduate degree focused in biostatistics.

In pharmaceutical companies such as Momenta, what is the place for statistical analysts and data scientists? I have long wanted to work in a setting such as the pharmaceutical industry, however my skills differ much from a chemistry or biology training.

Thanks again!

mostslycooper

Statistics is a very important part of biosimilars and, in fact, all of the analysis that I have done over the years. You do not necessarily need to have skills in chemistry or biology as long as you are willing to work with others in helping understand their problems. One of my earliest successful papers came in working with a PhD in Physics and Statistics on a chemical problem.

Hi Joseph, and thank you for doing this AMA.

Looking at Momenta's pipeline, I see that your furthest advanced biosimilar product is an Adalimumab (Humira) biosimilar. I was hoping you could help me understand a few things about the biosimilar business model:

1. It seems that a number of companies have already made and received approval for Adalimumab biosimilars (including Amgen). How do you gain market share in a market like this, where multiple companies are already marketing the same product?
2. Humira is approved for multiple indications. Would any Adalimumab biosimilar need to complete trials for each of these indications in order to be marketed to patients with each indication. If yes, can doctors just get around this by prescribing the biosimilar anyway?
3. There is some talk that the TNFα inhibitors are likely to be out-classed by anti-IL6R agents (i.e. Actemra, Sarilumab, Tocilizumab). Where do you see this market going in the coming years? Will TNF-blockers always be first line for arthritis patients?

SirT6

I cannot speak for the business models themselves since I am only involved in development, but I think this will be much like the traditional small molecule generic markets where multiple companies will be approved for some product and will all get some market share.

Most chemists seem to do their undergraduate, graduate, and post-doc studies at different colleges. Why is that?

poverty-law

Good question. The real reason for this is that you get exposed to different people, professors, and even ways of looking at the problems that will benefit you long-term.

Hi Dr. Glajch. Thanks for stopping by. Here are a few questions of a more personal nature that you might find worth speaking to (or not, which is fine):

- What, if anything, are you doing in your personal life to combat the rise of the anti-science / anti-fact culture in the US? Ex. Participating in mentorship programs for disadvantaged youth, writing op-ed articles for mainstream press, participating in local school boards, etc.
- (Follow up to the 1st question) What, if anything, do you think the rest of us (scientifically minded, but not necessarily working in the industry) can do to help change the culture?
- Immigrants have always had a strong role in the science and technology sector. Many of the larger US companies already lobby to protect various Visas and government programs that allow easy access to educated/skilled immigrants. With the growing anti-immigration sentiment in the US, do you think companies should be pushing harder to ensure immigrants can (and want) to come here?
- What do you think will be the biggest/most impactful jump in medicine in the next 10-20 years (i.e. what processes or treatments will skyrocket in either efficacy or use in the public)?

Thanks for your time!

PenName

All very good questions. I have throughout my career tried to work with young people and other friends of mine to support science in general and chemistry in particular. Part of this involved sessions like this today, I am also part of an ACS Experts group that speaks with local schools, community organizations, newspapers, etc. Not as much as I would like, but we are trying our best.

Hello and thank you for taking the time to speak with us here today.

Do you have the opportunity to still be creative in the private sector? As scientists we often have questions of our own not directly related to what we are working on currently. Do you have the freedom to pursue anything a little differently or do you have to stick to what the company needs? Often new discoveries are made from unplanned experimentation.

Thank you again for your time, it's appreciated.

FillsYourNiche

Thank you for this question. Yes we can be creative in the private sector in a variety of ways. I have been fortunate enough to work for companies that have permitted some time for other exploration of ideas but often you need to expand your work time and effort to do this.

If a pharmaceutical company employee discovered an inexpensive one-pill cure for an illness that now requires lifetime, expensive treatment using other products owned by his company, what would the company do with the discovery?

In other words, how are situations which present a conflict between the employees' moral duty and their fiduciary duty handled?

Bonus question: Does your firm spend twice as much on marketing as on research? Supposedly this is the industry average.

scotchleaf

Not sure I can handle the first 2 questions, but the bonus question is easy: We are developing primarily complex generic drugs and biosimilars. These require very little marketing since the brand drug has already done much of it (besides, our company does not market or sell -- we use partners to do that). In summary, one of the nice things about our company and work is that we spend almost all our money on R&D to get approvals, so it is satisfying to know that we can save the health case system and individuals a lot of money and expand access by the work we do.

What is your opinion on the rise of CMOs (contract manufacturing organizations) within the pharma industry and do you see tech transfer positions increasing in demand over the next decade? Current Tech transfer scientist at Patheon.

Manglue

I think tech transfer and the oversight of that is a crucial part of what we do every day. In my job, I spend as much time with our CMOs and I do with my own employees.

What is your opinion on the super high drug prices that you charge in America? Do you think it is ethical or responsible as a medical practitioner?

What is it that you dislike about the private sector in general, and your company in particular?

RaveAndRiot

This is a very complex issue with no real solid answers. I would note, however, that a major reason drug prices are high in the US is that we are subsidizing the rest of the world where prices are lower. Whether you agree with this or not, it is reality today that many drugs would not be on the market without the pricing in the US.

Would you be willing to give an extremely brief timeline of your professional life?

I'm currently considering going back to grad school, and I feel like I'm almost too many years behind people my own age, many of whom are finishing up their PhDs. Looking at other successful professionals with atypical timelines has been helping my spirits greatly.

Nothing too in depth, just approximate years in each stage of life.

Thanks!

curledtoes

I took a more traditional route -- 12 years of secondary school, four years of college, three years to get my PhD (I was lucky there, had a great mentor). The worked at a variety of positions at DuPont and BMS for 28 years (never more than 3-4 years in the same job). Now at Momenta for 9 years. Hope this helps.

Thanks for being here.

What is your understanding of the industry's attitude towards mass spectrometric analysis/characterisation of oligosaccharides? Is it used already, or would the ability to sensitively isolate these to the stereoisomer be seen of much value?

I will begin research soon, but feel supervisors often overstate how impactful their work might be.

Wakewalking

I think that is an open question. It will depend on whether the different structures that can be seen or identified have a meaningful clinical effect or not (safety, efficacy, or immunogenicity, for example). We won't know until we look for it.

What are the pros and cons working as a chemist in the private/industrial sector? How is like in a day's of work?

Agent_Pickles

I really enjoy working in the private/industrial sector for a number of reasons. I have always been involved in making products or services that help people whether it be chemicals, pharmaceuticals, or other products. In addition, the day's work is never boring and the private sector offers the opportunity to be involved in a wide variety of projects and problems.

What's the safety culture like in the non-academic world? There's a really big push in the UC system to be safe these days.

arden13

I started my career at DuPont and I can tell you that safety was THE top 3 on a list of 2 top priorities. And it became very important to those of us who worked there.

Hello Dr. Glajch,

I'm currently an undergraduate Biochemistry student, and I plan to pursue a graduate or even a doctoral degree. What helped you decide your focus? Every day I learn of more and more possible careers in the biochemistry path and speak with a mentor that works in industry pharmaceutical development.

With so many possibilities, I always find it fascinating to learn how scientists come to choose their path.

misterpistachioman

Interesting because I just answered a similar question today to a group of high school students. I took a lot of different science-related courses and discovered that I liked chemistry and math; analytical chemistry was the natural intersection of these two for me.

Hello,

What would you tell a young student (sophomore in high school...) that is considering entering the biochemistry field? What to study....college major...choice of school... any advice is appreciated.

magical_pixie_horse

I think it is great for you to be thinking about this already. An obvious major would be biochemistry or biochemical engineering -- as for schools -- there are many that are good. I would encourage you to visit as many as possible in your search (both public and private). You will know when you feel

comfortable at a certain place.

Just out of curiosity, how closely were you involved in the development of Sandoz' biosimilar for Copaxone, Glatopa?

_Shin_

So it is a matter of public record that I was heavily involved in that development and have spoken about it at numerous conferences. One of the most challenging and satisfying parts of my professional career.

Hello Dr. Glajch

I am a young analytical chemist working in the field of 2DLC. I am thinking about starting a consultancy to develop 2DLC and LCxLC methods for companies such as yours. Are you familiar with the technique? Do you see it play a role in your companies analytical arsenal in the future? What are the major hindrances for your company to adopt the instrumentation/methods?

Rikkid6

Good question. yes, I am familiar with these techniques and have used them a bit in the past. I think they will be important in the characterization of complex drugs or mixtures, but probably not for routine release testing or monitoring.

Thank you for doing this. I'm wondering how you think the approval process can be improved for biosimilars? Also, do you think the recent surge in newly patented biologic therapies is because of the complexity of the approval process for biosimilars (thereby effectively extending a patent lifespan)?

omgqftbbq

I think the approval process can and will be improved. I think we all need to understand that we in the US are early in this complex development and approval process. Both companies and regulatory agencies are still learning what is and what is not needed for a good submission and approval. I believe that this will get better with time (soon, I hope)!

Hi Doctor, thanks for doing the AMA.

What are the benefits of biosimilars as opposed to more conventional medications? Are there any approved biosimilar products available that you helped create?

alnitak

Biosimilars are intended to be additional drugs for those biologics already on the market (in the same way that generic drugs are to the original small molecule drug). A major benefit should be lower cost to patients due to increased competition which creates benefits both to current patients and expands use to patients who cannot afford the higher cost of the original drug. I am working on biosimilar products, but none has yet been approved

Given how biosimilars were just given a path of approval by the ACA, and those currently in legislation

are seeking to repeal the ACA, what will happen with this research and field should it end up being repealed and replaced?

chubimaster343

Good question. It is very likely that the entire Affordable Care Act will not be repealed and in the view of most in the industry, it is highly unlikely that the biosimilars pathway will disappear.

Hi Dr. Glajch! First, I wanted to thank you for your work. I have severe to moderate Rheumatoid Arthritis and taking Humira pretty much gave me my life back. I would like to understand more about how biosimilar medicines like mine work. I've tried looking up a few scientific papers but without a medical or chemistry background they don't make a lot of sense. Could you recommend any resources for someone who wanted to understand more about how biosimilar medicines are made and how they work? Thank you.

lava_is_hot

I would recommend getting in touch with a patient advocacy group in the area that can often provide good resources and knowledge for the non-science based patients. Google RA patient groups and I am sure you will find some good hits.

When a pill that is dosed at 20mcg (for example) is manufactured, do they make a large batch of filler, add the active ingredient at the proper ratio, and hope that 20mcg is in each pill instead of 18mcg in one and 2cg in another? Or do the measure out 20mcg for each individual pill and insert it directly into the filler for that particular pill, thereby insuring each dose is exactly 20mcg?

mrwhibbley

I do not have specific experience with pills, but in general a pharmaceutical manufacturer will make a large batch (which should be homogeneous) and then dispense into individual pills, vials, etc.) so that each unit should have the same concentration of active drug. In order to ensure that this is happening, multiple tests are done on the final product to demonstrate uniformity across all units or pills.

Thanks for doing the AMA! In your experience, how similar to the innovator molecules do biosimilars have to be? Identical in every assay? Or are there some assays in which variation is acceptable?

I've always wondered, have you ever heard of anyone degrading a biosimilar to match an old innovator product in terms of oxidation, deamidation or some other metric?

CaptObvious1234

A very good question that we in industry and our colleagues in the regulatory agencies such as the FDA are grapping with every day. There will always be some variation, both with the original biological drug run-to-run and with the biosimilars. We need to assess how critical those differences are and, if they could have an affect on safety or efficacy, how to mitigate those differences.

Dr. Glajch what is your take on the application of Quality by design principles being implemented during product development. Where do you see it going? are more and more companies implementing them? I have completed my Masters in QbD in UK recently and i am deciding if i want to do a PhD in pharmaceutical technologies or work. Thanks for your time.

iwantitritenow

QBD principles are definitely getting more use in the pharmaceutical industry in the past 10 years and I see it growing even more as we examine more complex drugs.

How important is having programming, coding, and data analytics skills (SAS, R, Python) in helping analyze pharmacological results and in the pharmaceutical industry in general?

nel_wo

Those programs and skills are vitally important to what we do, especially in a company like ours that thrives on analytics and data analysis.

Can you give us an idea in differences in R&D costs in making biosimilars in lieu of de novo drugs? And if you could talk about the differences and challenges of walking these through the FDA process versus the EMA approval process that would be awesome.

Thanks for doing the AMA.

hawkeye807

The R&D costs for biosimilars should be lower than original rugs primarily because of the lower need for clinical studies which are expensive themselves and require many batches of material to be made. As far as the FDA and EMA approval processes, this is a work in progress. There have always been differences among various regulatory agencies that those of us in the industry have had to work on; neither is "better" they are just different.