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In this episode, Taren Grom, Editor of PharmaVOICE magazine, meets with Lindsay McNair, M.D., Chief Medical Officer at WCG.

Taren: Dr. McNair, welcome to the PharmaVOICE WoW podcast program.

Dr. McNair: Thank you for inviting me.

Taren: It's our pleasure. Lindsay, you are the chief medical officer of WCG and an adjunct associate professor at the Boston University School of Public Health. You are a busy lady. How do you balance it all?

Dr. McNair: Well, I think sometimes better than others. I think probably struggling with the same work-life balance issues that a lot of people struggle with, and I think a lot of it is just deciding what's most important to me and then trying to make time for those things that are most important and that may change day to day, but sometimes the balance works better than others.

Taren: I think that's a very honest answer because you can have it all, it's just you might not be able to do it all, right?

Dr. McNair: Well and you may not be able to have it all exactly at the same time.

Taren: I think that those of us who are in an executive role, who have family, who have friends, who have demanding jobs struggle with this quite a bit. Thank you for your really transparent answer there.

As part of your role at WCG, you are charged with developing strategic partnerships with pharma biotech companies for comprehensive ethical and clinical services. You also oversee a group that provides consultation on HRPP assessment and transformation, ethical trial design, protocol development, data request review and data transparency guidance and the development of ethical clinical research policy and practices.

Talk to me about your role and where you see some of the biggest opportunities and challenges in terms of the clinical trial process in terms of clinical services.

Dr. McNair: Sure. What you described is kind of a lot of fancy words, but mostly what I do and what I'm privileged to do is to be able to work with the companies and the clinical sites that are sponsoring clinical trials, conducting clinical trials, working on clinical research and working on the developments of new therapies. Really, what I see my role is, is to try and facilitate the conduct of that research so that it can be done efficiently and effectively but also with real scientific rigor and in a truly ethical way. And what I find is, is that pretty much everybody working in the research enterprise, the biopharma companies, the investigators, certainly the participants of research studies, all want to do kind of the best, most ethical job that they can.

It's really both interesting and fun, kind of, to be able to work with all these different stakeholders and sometimes help them meet each other and work together, but really to try and create systems and processes and policies that help us all to move the clinical research world forward so that we can get to decisions about investigational agents more quickly and advance those most promising ones into the clinic most quickly where they're really going to be of benefit to patients.

Taren: With ethics being such a big part of your focus, how do you think the industry can do a better job at communicating in a credible in a forthright way with its stakeholders, particularly patients?

Dr. McNair: I think that's really a tough one and it depends who we talk about as the industry. If we mean the biopharma industry, it really is a challenge for people in that industry. I'm part of a group called the bioethics bio-industry consortium. It's a group of bioethicists who work for pharma companies and deal with the bioethical issues that come up as part of drug development. One of the missions and goals of that group is to make more visible the fact that there are actually bioethicists within biopharma companies helping everybody to try and do the right thing.

But we had a phone call very recently and we were discussing the fact that the public's opinion of the biopharma world is so negative and that they really feel that that there is not a lot of ethical consideration given to what pharma companies are doing and no separation between what they see as kind of marketing and pricing issues and drug development issues. It's an uphill battle to show that ethics is really an important part of what people in clinical research do every day and that it is something that they're always thinking about.

On the IRB side, the HRPP world – the Human Research Protection Program world – it's a little bit easier to talk about ethics because many people in clinical research understand that there are ethical committees that are responsible for the oversight of research and making sure that that research is conducted in a way that follows regulations but also prioritizes ethics and the rights and welfare of the participants of that research as well.

So it's a little bit easier to talk about on that side than it is on the biopharma side. But I have really never met anyone in my entire career who wasn't interested in making sure that they were doing the right and ethical thing as part of their clinical development work.

Taren: I have two follow up questions for you. One is what are some of the issues in terms of bioethics that you all contend with on the pharma side. And then the follow up to that follow up is what can the industry do to its reputation in terms of the public? What are some of the challenges you all face in terms of bioethics?

Dr. McNair: Well, there are lots of kind of ethical issues that kind of rise to the forefront at various times. One of the big ones that's getting a lot of discussion now is the issue of expanded access and right to try and people's right or ability to get investigational drugs if they have a very serious illness but they can't enter a clinical trial. There isn't one available to them or there isn't one that's right for them.

What is the responsibility or obligation of the biopharma world to make investigational products available to people and do people realize that those products are really investigational and most of them will never go on to become medicines. That's just kind of one of the issues that we struggle with both on the IRB side because we have to review the use of those medications because they're investigational that I know the biopharma world is struggling with as well.

Then there are lots of other things that come up. I have lots of conversation with sponsors about how to improve the informed consent process, definitely overlap with institutional review boards there as well. But biopharma companies are frustrated by how long the consents have become and how we feel like they're not really informative for research participants and how can we make that process better but still be compliant with all the regulations that require certain parts and certain pieces of information to be part of an informed consent document.

The second question about what we can do to improve the reputation of biopharma is a much bigger one and a much tougher one and one that I think a lot of people have been struggling with. There have been a few companies that have created some media campaigns to talk about kind of the scientists who do the work that they move into the clinic and how these are scientists who are dedicating decades of their lives to try and work on new therapies, to try to get some recognition for that part of the process as well. I'm not sure how much those things move the needle but I do hear people say that they've seen them.

I think there's so many efforts happening now with various companies getting involved in patient advocacy and working with patient advocacy groups to incorporate the voice of the patient much earlier in clinical development programs, getting feedback on study designs to see what's feasible, getting feedback about the endpoints that they're going to look at in their clinical trials, to make sure that they're choosing endpoints that are of interest to patients and not just those sort of interest to regulators.

I think those efforts are expanding and I hope that those will start to shift some of the public perspectives soon.

Taren: Thank you. I think those insights are truly helpful in understanding the complexity of the issue. Thank you for sharing those with us.

Switching tact a little bit here. You are an MD as well as holding a Masters in public health and a Masters of Science degree in bioethics. How have these experiences helped shape your career and perspective?

Dr. McNair: Well, I've had kind of an unusual career path. I went to a medical school that focused very much on training people to be primary care physicians and I decided to go into general surgery. I was kind of a failure of the career planning goals of my medical school. I trained as a general surgeon for several years and then did a research fellowship during which I ran a clinical research study and sat on the institutional review board. That was when I also got my Masters in public health concentrating in epidemiology, biostatistics and clinical trial design. When I went back into clinical practice, I realized that I actually liked research better than I liked clinical practice. I enjoyed trial design. I enjoyed trying to solve those questions. I enjoyed the regulatory aspects. I enjoyed the bioethical aspects of clinical research and drug development.

That was really when I kind of shifted careers and went to work in the biopharma field instead and did that for about 15 years at various companies; first as an employee and then as a consultant to many companies. Throughout that whole time, I stayed involved in institutional review board work. I was very interested in bioethics. I started a bioethics committee within one of the companies that I was working for. I really wanted to formalize my education in bioethics and also to show that someone who is in the pharma world actually could be trained in bioethics and have a formal education in that area and it wasn't just giving lip service to yes, we should do ethical stuff. And that was when I got my Masters in bioethics as well and that was with a concentration in research ethics.

That was kind of how I went along that career path and how the different parts of what I was doing and what I was interested in ended up shaping my career and then about 6½ years ago, I got the opportunity to come to WCG, the WIRB-Copernicus Group, which at that time was just an institutional review board company. We hadn't started the clinical service organization yet. It gave me a chance to combine the drug development background, the bioethics background, the clinical trial background and to really have a role in helping to advance drug development and clinical research in a different way.

People sometimes ask me if I miss practicing medicine or if I regret that I don't practice medicine anymore, and what I usually say is I actually still consider myself practicing medicine in a way. I'm actually still licensed to practice although I don't see patients, but I just practice on a

very different scale than I used to. I'm thinking about study populations and patient populations and therapeutic areas and remedies for therapeutic areas in a very different way, but I still think of this very much as being involved in the practice of medicine.

Taren: I think that's a really neat way to look at it because instead of seeing patients one-on-one you're seeing patients in the thousand. You can really affect change that can benefit potentially hundreds of thousands of patients.

Dr. McNair: I mean that's kind of how I like to think of it. I've often said that – you know when I first did Vertex and then as a consultant I worked on some of the first drugs that were approved as direct-acting antivirals for hepatitis C.

When I started and working in hepatitis C, cure rates were 25 to 40% with a year-long therapy that was absolutely terrible to tolerate. People dropped out of therapy all the time. The drugs that I worked on now have 99% cure rates for all different types of hepatitis C, 12 weeks of therapy, one pill a day. It has entirely changed that field. It has changed liver transplants because now infected organs can be used for liver transplant and the infection resolved.

It's changed so much, and I often say that one of the things I am most proud of in my entire career is the work that I've done those drugs and the effect that that has had basically on public health.

Taren: That's fabulous. Let's talk about your career going from a biotech company and now as part of WCG. What can each side learn from each other to streamline the clinical trial practice now that you've been on both sides of the table?

Dr. McNair: That's a good question. WCG has so many components. We have the institutional review board work and then we have our clinical services work that provides kind of very niche specific services that can help expedite the conduct of clinical trials and do it with really good scientific rigor.

A lot of that comes back to using data in the most effective way, using data to decide who your investigators are going to be, using data to look at whether or not you're seeing unusual placebo responses in your control arm, using data to select the best endpoint instruments, using data to have good endpoint adjudication in adjudication committees.

One of the things that we can do most effectively is just communicate back and forth between the people who are running drug development programs, which are sometimes small companies that don't have a lot of infrastructure and don't have a lot of resources but there are other sources of the data that they can take advantage of to help them make really wise decisions and efficient decisions in streamlining their clinical programs.

On the other side, in the IRB side, I think institutional review boards are best when they really understand drug development. Many institutional review boards really grew up in a very academic environment and still think of biopharma as kind of the bad guys and I think we really have moved away from that. We have lots of people who communicate directly with the sponsors of our studies and I think the more the IRB understand about drug development and drug development goals and why sponsors write protocols in a specific way, I think that that will help everybody to have oversight of the studies that is effective and rigorous but also doesn't create unnecessary roadblocks to moving studies forward.

Taren: Fantastic. I think you're right on both sides. I think that there is better communication; better understanding is all wonderful to move that clinical trial process forward, to make it easier for patients, to make it safer for patients, et cetera.

Over the years, you've obviously seen the evolution of how research is conducted particularly the concept of phases of research that came into being decades ago, but so much has changed in medical practice technology, in the therapeutic interventions that are being developed and the diseases themselves that are being studied.

Some say that the phase 1, 2, 3 paradigm is perhaps outdated with products being approved by the FDA based on the conduct of a single phase 1 study. From your perspective, what does this mean in terms of drug development and also from an ethical perspective? Can we get back to a one phase study?

Dr. McNair: Well, we already have, certainly in some cases. I mean, Keytruda, pembrolizumab's initial approval was of what was technically a phase 1 study although it was a phase 1 study with hundreds of people in it, but it was the initial study that started out looking at safety and then just kept adding cohorts to the study as the study continued all under off protocol until there was enough data in a specific population to support an approval.

I think especially in oncology, we are really seeing that phase 1, 2, 3 concept really kind of being left behind. We have basket protocols and umbrella protocols and master protocol designs, platform studies that look at multiple study questions within the context of one protocol. We see lots of sponsors doing staged phase 1/phase 2 studies and part of that is just because of the operational challenges of conducting research.

If you can start a study and then answer some of your questions, amend the protocol, continue the study, why shut a study down, close all the research sites, stop enrollment, write a new protocol, wait 6 months, qualify the sites all over again, initiate the sites all over again, start enrollment all over again, have new contracts and all of that still go through the IRBs all over again. Why not just do that in one whole smooth protocol rather than having that shut down and start up time in between each phase of your research and make it much more

efficient to get to next answer that will either propel that drug toward the clinic or stop development on that drug and put those resources toward something that's more promising.

But what those considerations then bring us an ethical issues as for one thing, everybody needs to update their patient facing materials because everybody's website still talks about phase 1 is when we look at safety and phase 2 is only start to look at efficacy and that's just really not true anymore, especially in oncology and rare diseases, but it also means that we have to be much more careful about things like the therapeutic misconception and the therapeutic misconception is an ethical concept where patients have difficulty separating the concepts of when they are getting medical care and when they are participating in a research experiment because clinical trials are essentially a research experiment.

It's really important – we don't want to take away people's hope that a therapy might work for them, especially if they have no other treatment options, but at the same time we have to make sure that people are truly understanding the potential risks and benefits of being part of research and understanding what that may mean to them, that many of these drugs just because it's a new drug doesn't mean it's a better drug.

Many of the drugs that start in development will not make it to the clinic and some of them could have side effects or safety issues that are worse than what's currently available. Just because something is new doesn't mean it's always better and I think those are kind of the educational challenges that we have, the informed consent challenges that we have as these paradigms of research change.

Taren: I think those are excellent points and for some for some patients, some of these new medicines that are coming out and even though they are investigational, I see their last best hope for something. How does that come into play?

Dr. McNair: No, that's absolutely true. That's kind of – the therapeutic optimism is the idea that we don't want to take away people's hope that this might – it's a phase 1 study. It's very early. We don't know anything about this but it might work for you but at the same time, make sure that those hopes are tempered with the realism that it very well may not work for them.

We don't want to be paternalistic or maternalistic, parentalistic and telling people what they should do or what they should think but we also know that when people are desperate and people who are very ill or have a family member who's very ill can be desperate for therapies. We have to make sure that what they're presented with are options that are good for them.

I've had patients say to me 'I don't care, I'll sign anything. I don't care what the informed consent says this is the drug that's going to save me. I know it will. I just need to get it. I don't care. I'll sign whatever you want.'

It's so difficult. It's gut-wrenching because you know that they really don't have any other options. There are no other therapies. They may have tried other therapies that have already failed but at the same time when someone says I know this is the one that's going to save me. It's a really difficult conversation.

Taren: Your training as a physician has to come in handy at that point to be able to be empathetic but yet also very clinical in having that conversation because as you well know it may not be the cure-all that they think it is, you temper that hope without extinguishing it but to give them the options. Those are very tough conversations to have.

Dr. McNair: That's really the challenge.

Taren: You talked a little bit about basket studies and platform studies. What are some of the biggest clinical research trends you're tracking right now or two of those counts among them?

Dr. McNair: I think some of the biggest trends that we're tracking right now; I would say there are probably two. One is that we see more and more protocols of kind of non-traditional designs. Some of them are the master protocols, the umbrella protocols, the basket, the platform. Some of them are just creative new don't really have a name study designs. Some of them are oncology studies that start with small cohorts and then are designed to expand as they start to see signals of efficacy.

We're seeing more and more creativity and innovation in the designs of studies. I would say the other big trend that we're seeing is real – and I hate to call it a trend because I hope it's not going to be a trend that then goes away, but a movement toward this is the accepted new normal is the involvement of patients and patient advocates in the drug development process.

Getting people involved very early, not just having them look at a finished protocol and look at a finished consent, but talking with patients and patient groups very early to say this is what we think we're going to study for the outcome. What's important to you? What would make the biggest difference in the quality of life for you? This is what we're thinking about for a study visit schedule, does this seem feasible to you? Is this something you would be able to do or be willing to do? Is this way too many times coming into the clinic?

What are the things that we haven't thought about that impact you as someone who knows the disease and the disease process much better than we do? I think that's really the other big thing that we're seeing quite a bit.

Taren: I think it's interesting to hear the words innovation and out of the box thinking, not in a negative way about, in terms of clinical protocol design because they've been designed for so long the same way. Creativity in this instance is really a good thing.

Dr. McNair: It's a good thing and it's also – biopharma tends to be a very risk-averse field. Everyone wants to be compliant with the regulators and sometimes in multinational programs there are lots of regulators to consider. Kind of the safest way to do that is to do what you've done before you know was accepted rather than to try and step out of the box and say we're going to do this an entirely different way.

It's tricky and it has been slow adoption of some of these things. I've told people I'm old enough in clinical research to remember years ago when we went from paper case report forms to electronic case report forms and that the data management teams at the company that I was at then fought like anything to not have to be the group that piloted the electronic case report in their study.

Everyone wanted to stick to the paper because the paper was comfortable. They knew how to use the paper. It was a yellow page and a pink page and a white page and they knew what to do with each one and everybody was used to doing that. Nobody wanted to be the first to pilot the electronic a report form and now there's still paper used more than you would think but now the electronic case report forms are standard, but it was a hard sell to get people who are not comfortable with the way they were doing things to make that switch.

Taren: Change is hard. But when we look at the new sciences coming out it almost demands new ways of thinking.

Dr. McNair: I think that's absolutely true. Yeah, it really does. When we look at some of the therapies for rare diseases, we can say well you should never do your first in human study in children. You should always give drugs to adults first and get data and then you can move into children and that's been our paradigm for a long time.

Well, if you have a rare genetic disease that affects very young children who don't live to be adults, then that doesn't make any sense, because you'll get safety data in the adult population who will never get the drug that doesn't transfer to the children.

Taren: Exactly.

Dr. McNair: We have to think about first-in-human studies in newborn babies that may be something that we have to think about now. As you said change is hard, but the new therapeutic areas, the new therapeutic innovations are going to force us in those directions.

Taren: Absolutely. Again, it goes back to that empathy and to be a parent of a child with a rare disease who may not live past the age of 4, and then there could be something that could potentially help them but they're blocked from that treatment because of an outdated guideline or regulation.

Dr. McNair: Yeah.

Taren: That's why those parents are warriors, right?

Dr. McNair: Yes and often it's not guidelines or regulations, but it's just "the way we've always done things."

Taren: Sure. You are one of the handful of women, Chief Medical Officers and as such you really are truly a role model to many women. What does this mean to you? How does that shape who you are and how you communicate with others?

Dr. McNair: Well, that's an interesting question. When I was a surgical resident there were not very many female surgical residents, and I remember I was in the emergency room and picked up the next chart on the pile, went into the room where the patient was and introduced myself and the patient said oh, no, sorry. I don't want a woman doctor. I want – I'll wait for the male doctor.

I left the room and I remember thinking like that's not my problem. That's his problem. It's not my problem. The nurse said to me 'why are you out here so fast,' and I said 'well because he doesn't want to see me, he wants a male doctor.' And she said 'oh no, no, no,' and she took the chart and walked me back in the room and basically told him that this is what he was getting and he could like it or he could leave.

I was his doctor and we got along fine, but I think being in an executive role as a woman is actually – I can speak out about things that other people may not be able to speak out about because I am a little more protected almost. I can say we really need to have more women on our board of directors and there may be younger women in our company who are thinking the same thing but can't say that to the CEO and I'll say it to the CEO because I can get away with it. I'll say that. That's my role.

I've gotten to this level and one of the things I'm going to use it for is being outspoken about the fact that we need more women on boards of directors. We need women in leadership roles. We need diversity in boards of directors and diversity in leadership roles. If I can use my position and the protection that comes with being in an executive position to say that, I will definitely do that.

But I also feel like I have a responsibility to act as a mentor to younger women within this company, within this industry, wherever it is. I get a fair number of calls from women who are practicing medicine but are unhappy and to get connected to me by various people and they reach out to me and say I hear that you left the medical practice and you're happy, can I talk to you?

I ended up talking to a lot of people who are thinking about leaving clinical medicine for other careers and I'm happy to do that. I think it is a failure of career planning in medical school that we teach people that if you do not practice clinical medicine, you are a failure as a doctor. That's one of the other areas where I see my responsibility.

Taren: How would you define your leadership style?

Dr. McNair: Well, as I've said I trained as a general surgeon. One of the things I have to be careful about with my surgical style is that I can still have a very much a surgical personality. I try to manage my leadership style so that my perfectionism is not pushed down on to other people.

I'm very careful about trying to give compliments, trying to support people when they've done something good. I try to get feedback even though I may make the ultimate decision on things but it is evolving and I think it also depends who I'm with and who I'm working with on the rest of the team as to what my leadership style is that day.

Taren: Well, I think that's very insightful. I think that's also very transparent. It shows great insight is to understanding who you're dealing with and who you're working with because not everybody can be managed the same way from the same position.

Dr. McNair: Yes.

Taren: Kudos to you. In that vein, how do you define success to yourself? You've obviously reached a pinnacle of your career. There's more things that you obviously are doing and have ambition for but how do you define success for you?

Dr. McNair: Well, it's an interesting question. I don't know that I've ever specifically tried to define it. I have work that is challenging and interesting to me. My family is happy and healthy. I have a good core group of friends that are important to me and supportive of me. That's pretty much all that I'm aiming for.

Taren: That's all good. Nothing bad about any of that. That's fantastic.

Dr. McNair: I've never had a goal to get to a specific title or anything like that. I think it's really just the more general stuff.

Taren: I think happiness is in success is what you surround yourself with and not by definition, your definition of success, which I think is wonderful. There's nothing wrong with having a happy, healthy family, a fantastic career and great friends. To me, you ticked all the boxes.

Dr. McNair: Yeah. It's pretty good.

Taren: Yes, it is pretty good. Finally, this is our WOW Woman of the Week podcast. I need to understand, know from you what is a wow moment that shaped your career? Can you pinpoint one?

Dr. McNair: I think probably the moment that has most shaped my career is when I decided to leave clinical medicine and go into research. It was a decision that I made when I was a senior surgical resident, when I was on call one night and I got called to see a patient and I had come back from my research fellowship and my time doing research and everyone kept saying aren't you looking forward to getting back into the clinic? Aren't you looking forward to getting back into the OR? I realized that I actually wasn't looking forward to getting back in the OR, at least not the way you needed to look forward to it, to make a career of surgery and I think the moment that I actually said to myself I've invested years toward this but I don't have to keep doing this if this is not the right path for me and I can do something else, was really the most pivotal moment, the most wow moment.

Taren: What a brave moment, if I may add.

Dr. McNair: It's very scary, very scary moment, actually, but yes.

Taren: Yes. Yeah, but brave to be able to synthesize that and say despite all that I've given to this and all that could be ahead for me, to understand oneself to say no, this is not going to make me happy.

Dr. McNair: Yep.

Taren: That's incredibly brave, not everybody would have taken that step.

Dr. McNair: Well, thank you.

Taren: I can't tell you how much I've enjoyed our conversation. Thank you so much. I really do feel the empathetic nature that you have when you talk about patients and you talk about having those difficult conversations, especially for those who are the last resort for a therapy. That's just – it's heart-wrenching and being able to have those conversations in a way that is thoughtful yet clinical and to continuing what you do.

Dr. McNair: Well, thank you very much. I consider myself very privileged to be able to do what I do, but it is something that I enjoy as well. Thank you for speaking with me today.

Taren: It's our pleasure and thank you for being part of our WoW podcast program.

Dr. McNair: Thank you.

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