

## EPISODE 3 :: PROBIOTIC MANUFACTURING & QUALITY

**Featuring ::** Adam Baker, PhD; Karyn Wulf, MD, MPH

### TRANSCRIPT

**Maura:** Hello again, listeners. Welcome to our third and final episode in a podcast miniseries on probiotics. If you've been listening all along, you've heard [episode one](#), which focused on probiotics and their mode of action. And [episode two](#) addressed the differences among probiotic strains and considered the clinical implications for each. If you missed either of those episodes, I really encourage you to take a few minutes to listen. They're both less than 30 minutes long and they're truly worth your time.

**Maura:** I'm Maura Bowen, podcasting for Abbott Nutrition Health Institute. I'm back with the esteemed Dr Adam Baker and Dr Karyn Wulf, who will speak today about probiotic manufacturing and quality. If you haven't met Dr Baker, he is Director of Science, Human Health Innovation for Chr. Hansen in Hørsholm, Denmark. And Dr Wulf is a Medical Director of Pediatrics here at Abbott, as well as a frequent contributor to the ANHI podcast. Dr Baker, Dr Wulf, welcome back!

**Dr Baker:** Thank you, Maura, it's great to be here.

**Dr Wulf:** Thank you, Maura.

**Maura:** By now, you both know the drill—I really think it helps our listeners to hear a bit about your backgrounds before digging into the subject matter. Dr Baker, would you like to start?

**Dr Baker:** Great, yeah, hi. So, my name is Adam Baker, and as I said, I'm the Director of Human Health and Science at Christian Hansen. I've been very lucky for the last eight years to be studying the microbiome, or more specifically, the role of the bacteria and what they play in the development of the microbiome through the life stages. Before that, I had the privilege to work in the biotech and pharmaceutical industry for the last 20 years studying complex diseases and oncology, where I've been focused on therapies and diagnostics to support patient diagnoses and treatments. It's great to be here.

**Maura:** Excellent, thank you. And you, Dr Wulf?

**Dr Wulf:** My name is Karyn Wulf, and I am a general pediatrician with 18 years of clinical experience, and I am currently the medical director of pediatrics at Abbot.

**Maura:** Thanks to you both for the helpful background. Now, a note to our listeners: Like last time, we're dialing in for today's episode. Dr Baker is calling in from Denmark, and Dr Wulf and I are still in social distancing mode, so we're ringing in from Columbus, Ohio. I say this to let you know our recording quality may sound different from what you're used to hearing. Secondly, we're going to stick with the format we established in our first series episode so we can get a dialog going between our two experts. Dr Wulf will do the interviewing with added commentary, and Dr Baker will provide his insights.

**Maura:** Dr Wulf, with that said, the microphone is yours.

**Dr Wulf:** Thank you, Maura. So, for this episode, I really wanted to focus on probiotic safety and learn a little bit about the manufacturing process. Dr Baker, thank you for being here again. I'd like to start off today's discussion by asking a question about the safety of probiotics, specifically some of the questions that come up regarding its clinical use. How do we know that probiotics are safe to be used, specifically whether or not they contain plasmids or if they have antibiotic genes that are transferrable? How do you verify that the probiotics Christian Hansen makes are safe for use?

**Dr Baker:** It's a great question and I've actually combined some of the science we focus on at Christian Hansen, and then move us into the safety and production. We look at each of these strains—all our strains are sequenced genomically—we get full genome sequences and then we're able to analyze them, and we're able to check and make sure they contain no antibiotics resistance genes or no mobile elements. And that is always done before we move forward in our research, even, because it's very important for us to make sure these probiotics, these strains, are safe for human consumption.

**Dr Wulf:** And along those same lines, one more question: How do you know that these strains stay the same over time? How do you know the strains you use are stable?

**Dr Baker:** That's also a very, very important point and very, very interesting. We actually published a paper earlier this year studying the stability of the genomes of our strains through our production process and over time, and we actually have steps in place in production that control for and make sure that we actually have the same strain, and there's no opportunity for that strain to drift genomically. And we have to have some sort of quality control, so we take pictures or look at the strains within the gels that are being grown in the factories to ensure that they still are the same strain—there's no contamination, no changes in those strains.

**Dr Wulf:** You told us several reasons or ways that the strain stability and safety are measured at Christian Hansen. Could you talk to us a little bit about how the probiotics strains or colony-forming units are counted and how you can be sure the correct number of probiotics are in the packages?

**Dr Baker:** It's key that you actually have a live bacteria in your product, so you should actually always be checking with the manufacturers and making sure that the product is describing what is happening with the colony forming, and it's at the end of the shelf life, to ensure that the products you're using in the clinic or in the pharmacy actually have the numbers of bacteria present that should be there, and they will be alive when you're actually using them. In terms of therapeutic windows, we've described this before that there's different ways—and we actually have clinical efficacy to prove that the doses we're using are correct. And then you start to shift over and think about production. Production quality, CFU and validated counting methods to ensure that you always get an accurate number of colonies, an accurate number of how many bacteria are alive, and you get that every time.

**Dr Wulf:** So, for those of us who are a little less knowledgeable about the process. We know that probiotics are living microorganism; can you describe how they're counted and how they're kept alive and don't grow while packaged?

**Dr Baker:** Yeah, this is where we start to use phrases—things like “Industry-validated” methods for counting the bacteria. It can't just be that you count the bacteria on the plate—these colony-forming units—one way, and in another factory or another lab or somewhere else, you count them another way. You have to have industrial methods and you have to consider that the counting of the product of the bacteria is just a final step in so many things within the production process. We spend a lot of time focusing on setting up all the systems that we can have this fantastic production; control fermentation and growth of the bacteria; the bacteria have to be in the best state and the right stage of their growth, and then we have to take them through these processes where we process them further—most of the time we actually freeze-dry them—so that they're alive and optimally alive so we can keep

them on the shelf and have a stability. And that's where we start to describe that we then count the strains. That we then have this CFU count and we can tell you that the strain is viable and will be stable and will be this number of colonies after 18 months of this certain date.

**Dr Wulf:** You mentioned contamination. How can you be sure there aren't other microbial contaminants in your product? I'm sure you're aware there had been a study of probiotics available as dietary supplements in the US that noted significant quality issues: either the wrong colony-forming unit counts, missing the probiotics that were listed, or even containing other probiotics that were not listed. What's different about the way Christian Hansen manufactures these strains?

**Dr Baker:** Yeah, thank you for the question. And all I can say is yes, I've heard of these studies and all of these products as well, and it's really surprising and disappointing. What I can say is that absolutely everything is different at Christian Hansen, and that's what we're proud of. We've taken so many steps to ensure that the correct bacteria are present. We touched on that in the last answer. We touch on it every day in our production systems. We always are working to make sure there's no contaminants in the products. This is a challenge. When you're growing microorganisms, you're growing bacteria, how do you ensure this doesn't get contaminated with other products? We work at the food supplement level, then we work at the higher level which is called infant nutrition level, and then we've even developed new levels of safety for working with the preterm babies and the products we're making and the strains we're using in these very, very vulnerable babies. And we are using multiple control steps and contaminant testing. We were industry-leading before we even developed these new controls, we're now using for the preterm baby quality. Just to take you through it, it really is a whole new level. We test against entire panels of microbial contaminants each time and at each step in the production process to secure that the product is safe for preterm infants. We have what others simply do not have: environmental monitoring prior and post every production step as part of the product release packages.

**Dr Wulf:** You mentioned that Christian Hansen was already an industry leader in product safety and quality before the additional testing for the preterm infant. Can you describe some of those quality standards that make Christian Hansen so different?

**Dr Baker:** Yeah. All of this is made possible because of the production facilities we have. The whole systems; the whole way they're set up; the qualified production equipment and software throughout our factories; the validation of our processes to ensure the safe and clean products. You have to simply see the factories and see the kilometers of pipes and cleaning systems that are all closed-circuits that are making sure there are no opportunities for any types of contaminants to enter the systems.

**Dr Wulf:** So, one of the questions that comes up when considering the use of a probiotic in the hospital setting is the possibility of surface contamination and the potential spread of a probiotic organism to unintended patients or the person mixing and administering the probiotic. Can you talk a little bit about what happens to different probiotic strains once the packaging has been opened?

**Dr Baker:** Yeah, absolutely. I think the first point is actually a minimal chance of contamination or spillage because with this product and these strains it's specifically designed with the package to be single-use and very easy to use. But then when we think about the strains, two of the strains are Bifidobacteria, and by definition, Bifidobacteria are anaerobic which means they cannot survive in oxygen. So, as you can image, if they were exposed and left out or somehow within a room, they actually do not survive very well at all, due to the fact they're used to being within you inside your body. All of these strains are safe. They're counted as probiotic strains, they give health benefits, they're no risk, but they're actually quite fragile in that environment.

**Dr Wulf:** Is there anything else you think clinicians should know about the safety of these probiotic strains?

**Dr Baker:** Clinicians really need to look at the specific strains that are being produced at the highest standards of

safety and quality. This is so critical when we're thinking about preterm infants. On top of that you have to as a clinician consider how the strains are working. Think about the scientific background—the science behind them—the mode of action and the description of clinical safety and efficacy. The safety and the quality of production is paramount, together with the science, the undeniable clinical science, the science behind that is what you need to look at and consider.

**Maura:** You both are fabulous, and we're really grateful you've been willing to take the time to help us better understand probiotics and the role they can play in improving overall health. Thank you again so much. We hope you'll join us again.

**Maura:** Listeners, my final notes today are for you. Both Abbott Nutrition Health Institute and Christian Hansen have a host of educational materials on our respective websites to help you learn more about some of the concepts we discussed over the past three episodes. Visit [anhi.org](http://anhi.org) today and click "RESOURCES" and then "KNOWLEDGE HUB" to find probiotic related content on neonatal health and the microbiome. And, be sure to visit the Christian Hansen Probiotics Institute—theprobioticsinstitute.com—to learn more about how probiotic strains can benefit the microbiome across the lifecycle.

**Maura:** Thanks everyone. Stay healthy and safe.