

# WHAT PROBIOTIC SHOULD I RECOMMEND TO MY PATIENT?

*Clinical Guide to Probiotic Products in Canada*

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# PRESENTER DISCLOSURE

- Presenter's Name: Dragana Skokovic-Sunjic
- I have no potential or perceived conflict of interest
- I have the Relationships with commercial interests:
  - AEPbio (Alliance for Education in Probiotics): Author, Advisory Board member

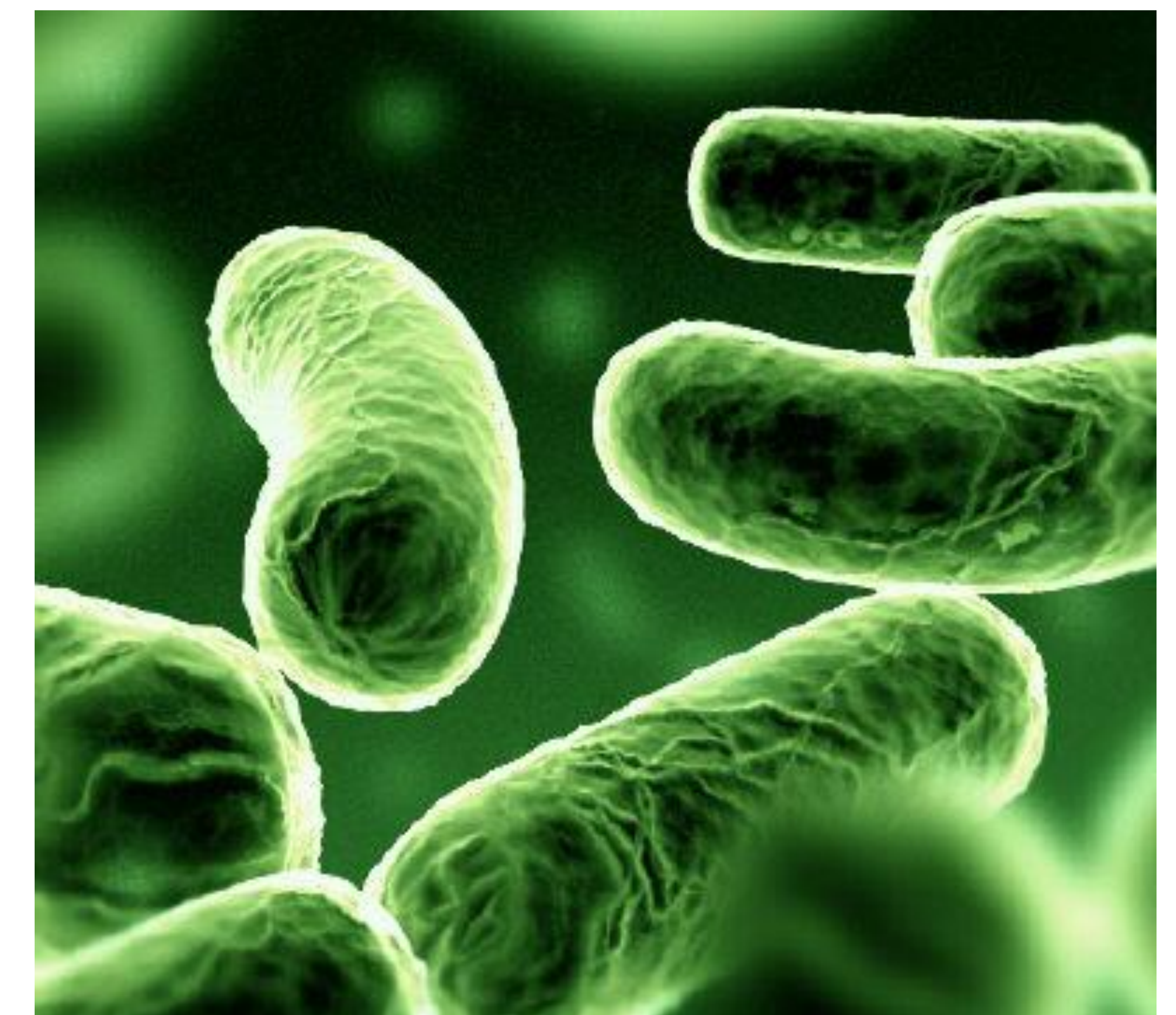
# COMMERCIAL SUPPORT DISCLOSURE

- This program has received no financial or in-kind support from any commercial or other organization

# PROBIOTICS : DEFINITION

Definition:

“**live** microorganisms which when administered in **adequate amounts** confer a health benefit on the host”



# PROBIOTICS : DEFINITION

*OLD* Definition:

“**live** microorganisms which when administered in **adequate amounts** confer a health benefit on the host”

*NEW* definition:

“**live** microorganisms **that**, when administered in **adequate amounts**, confer a health benefit on the host”



# CONSENSUS STATEMENTS

OPEN

EXPERT CONSENSUS DOCUMENT

## The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic

*Colin Hill, Francisco Guarner, Gregor Reid, Glenn R. Gibson, Daniel J. Merenstein, Bruno Pot,  
Lorenzo Morelli, Roberto Berni Canani, Harry J. Flint, Seppo Salminen, Philip C. Calder  
and Mary Ellen Sanders*

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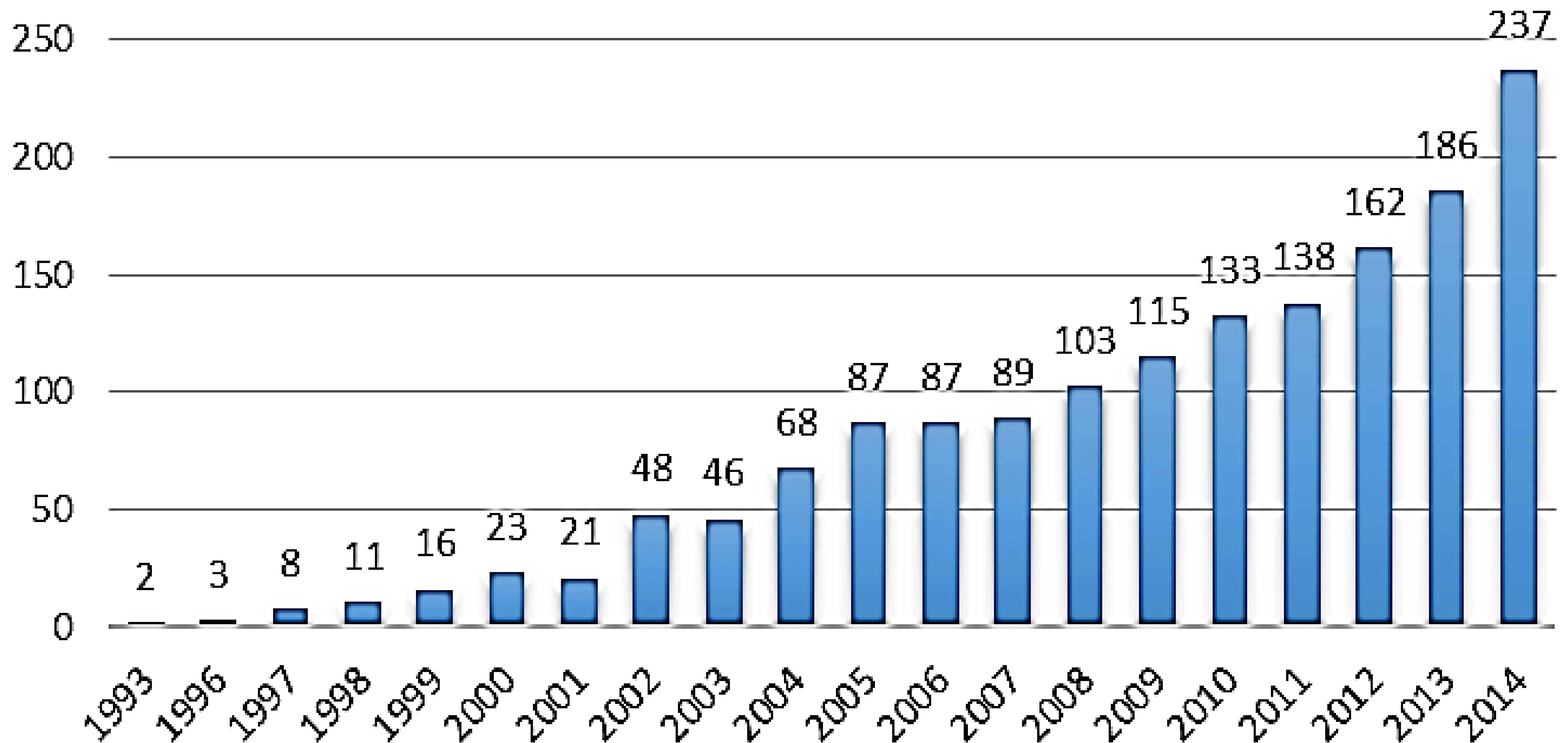
Let's eat grandpa.  
Let's eat, grandpa.

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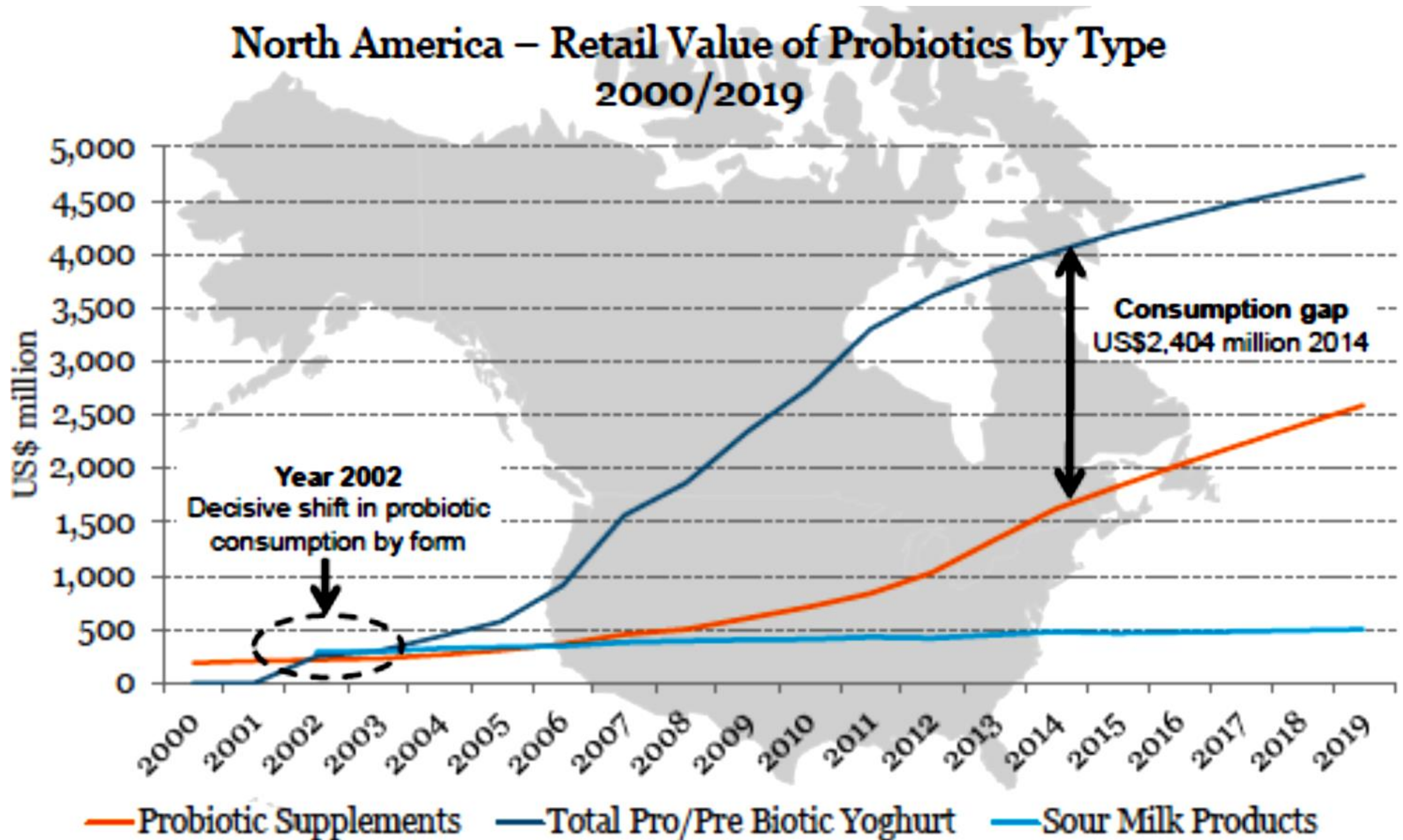
# CLINICAL RESEARCH IS EXPANDING

Search keywords: probiotics, clinical study, English language

## Number of published studies by year 1990-2014



# CONSUMER INTEREST IN PROBIOTICS





# WHY IS THERE DISCONNECT?

- Science 
- Popular demand 



# WHAT DOES OUR PATIENT SEE ON THE SHELF?



Photo: curtesy Iris Kracwchenko RPh

# HOW TO RECOGNIZE A TRUE PROBIOTIC

- ✓ Quality of the strain(s) of probiotic
- ✓ Synergy of the microorganisms, if in combination
- ✓ Guaranteed bioactivity, i.e. live and healthy microorganisms able to carry on the probiotic activity
- ✓ Protective environment: Microorganisms can provide maximum activity at the site of action
- ✓ Clinical research on the finished product has been conducted for efficacy and safety

# DO PRODUCTS WITH MANY STRAINS PROVIDE ENHANCED BENEFITS ?

- Adding extra strains to a proven formulation does not necessarily make it better (may interfere with the proven activity)
- Clinical benefits have to be proven for particular mixture
- Some strains are not recommended for human use

# DOES A HIGHER DOSE OF PROBIOTIC PROVIDE ENHANCED BENEFITS ?

- Calculated in **CFU** (colony-forming units)
- Not possible to determine a general dose for all probiotics
- Must be based on human studies showing a health benefit
- Varies greatly depending on strain and product

# SOME COMMERCIALY AVAILABLE PRODUCTS IN CANADA

<b>GENUS &amp; SPECIES</b>	<b>STRAIN</b>	<b>BRAND</b>
<i>Bifidobacterium lactis</i>	<b>CNCM I-2494</b>	Activia
<i>Bifidobacterium infantis</i>	<b>35624</b>	Align
<i>Lactobacillus rhamnosus</i>	<b>HA111</b>	Bacid
<i>Lactobacillus reuteri</i>	<b>DSM 17938</b>	Biogaia
<i>Lactobacillus acidophilus</i>	<b>CL1285</b>	Bio-K
<i>Lactobacillus casei</i>	<b>LBC80R</b>	
<i>Lactobacillus rhamnosus</i>	<b>CLR2</b>	
<i>Lactobacillus casei</i>	<b>CNCM I-1518</b>	DanActive
<i>Saccharomyces boulardii</i>	<b>Iyo</b>	Florastor
<i>Several genus and species</i>	<b>Several strains</b>	Probiac
<i>Lactobacillus plantarum</i>	<b>299v</b>	TuZen
<i>Several genus and species</i>	<b>Several defined strains</b>	VSL#3
<i>Bifidobacterium lactis</i>	<b>BB-12</b>	Yoptimal
<i>Lactobacillus acidophilus</i>	<b>LA-5</b>	

# CLASSIFICATION OF BACTERIA

(documentation on strain level required)

Genus

*Lactobacillus*

Species

*L. reuteri*

*L. rhamnosus*

Strain

ATCC 55730

ATCC PTA 5289

ATCC 53103

LB 21

# CLASSIFICATION OF BACTERIA

Is the strain really important?

Genus

*Homo sapiens*

Species

*Healthcare professional*

*Athlete*

Strain

Dr. Oz

Dragana

Wayne Gretzky

Michael Phelps



# CANADIAN REGULATIONS

- Health Canada has adopted the FAO/WHO definition of probiotics
- Probiotics can fall under the ***Food*** or ***Natural Health Product*** categories

**Health Canada website for approved claims:**

**NHP:** <http://www.hc-sc.gc.ca/dhp-mps/prodnatur/index-eng.php>

**Food:** [http://www.hc-sc.gc.ca/fn-an/label-etiquet/claims-reclam/probiotics\\_claims-allegations\\_probiotiques-eng.php](http://www.hc-sc.gc.ca/fn-an/label-etiquet/claims-reclam/probiotics_claims-allegations_probiotiques-eng.php)

# HOW TO FIND OUT WHAT TO RECOMMEND?



what probiotic should i use

Web

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About 2,120,000 results (0.44 seconds)



safe and effective probiotic

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About 784,000 results (0.61 seconds)



probiotics with clinical evidence to recommend to my patient

Web

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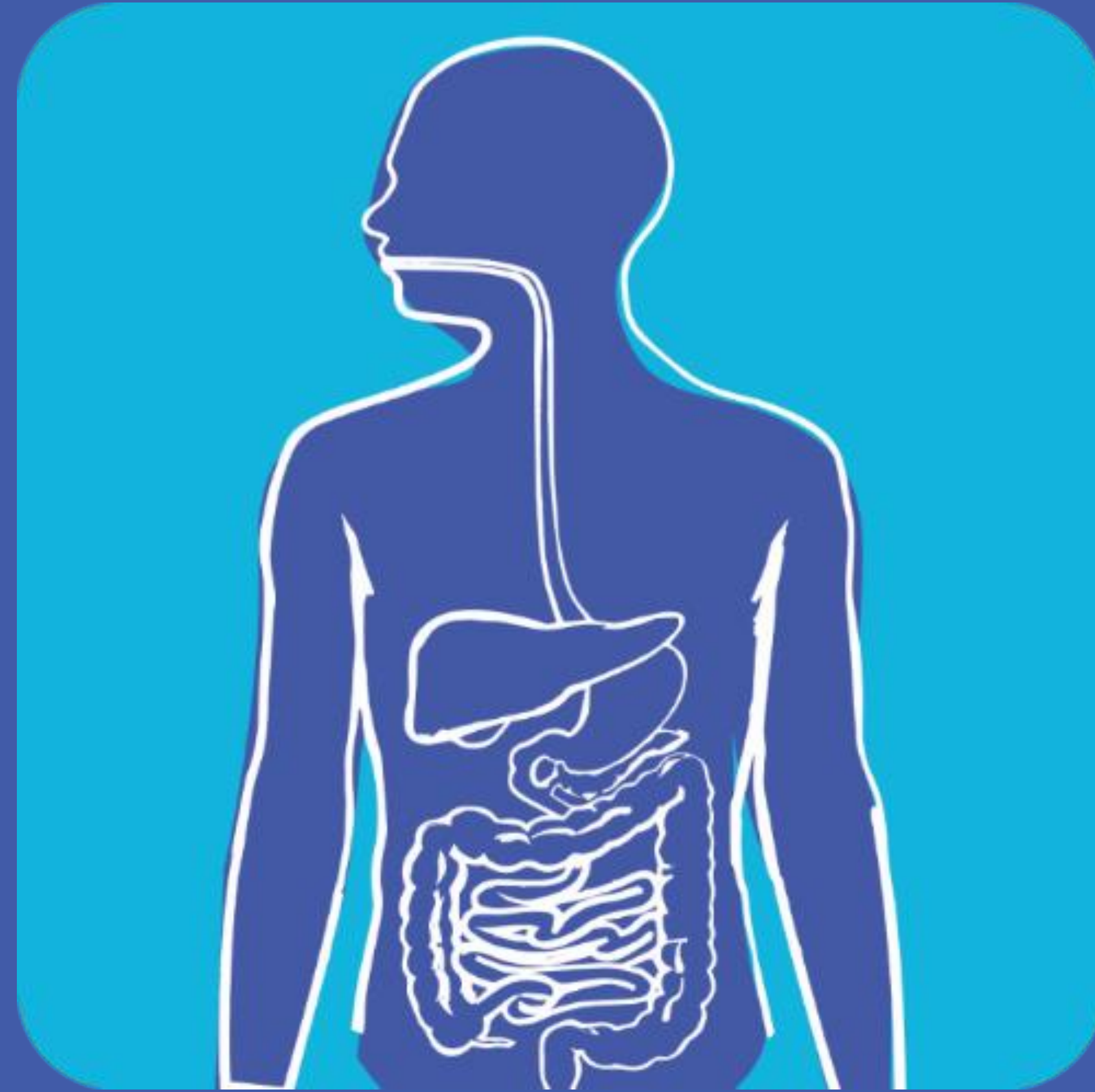
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**Clinical Guide to Probiotic Supplements  
Available in Canada: 2015 Edition**  
Indications, Dosage Forms, and  
Clinical Evidence to Date

Author: Dragana Skokovic-Sunjic BScPhm RPh NCMP

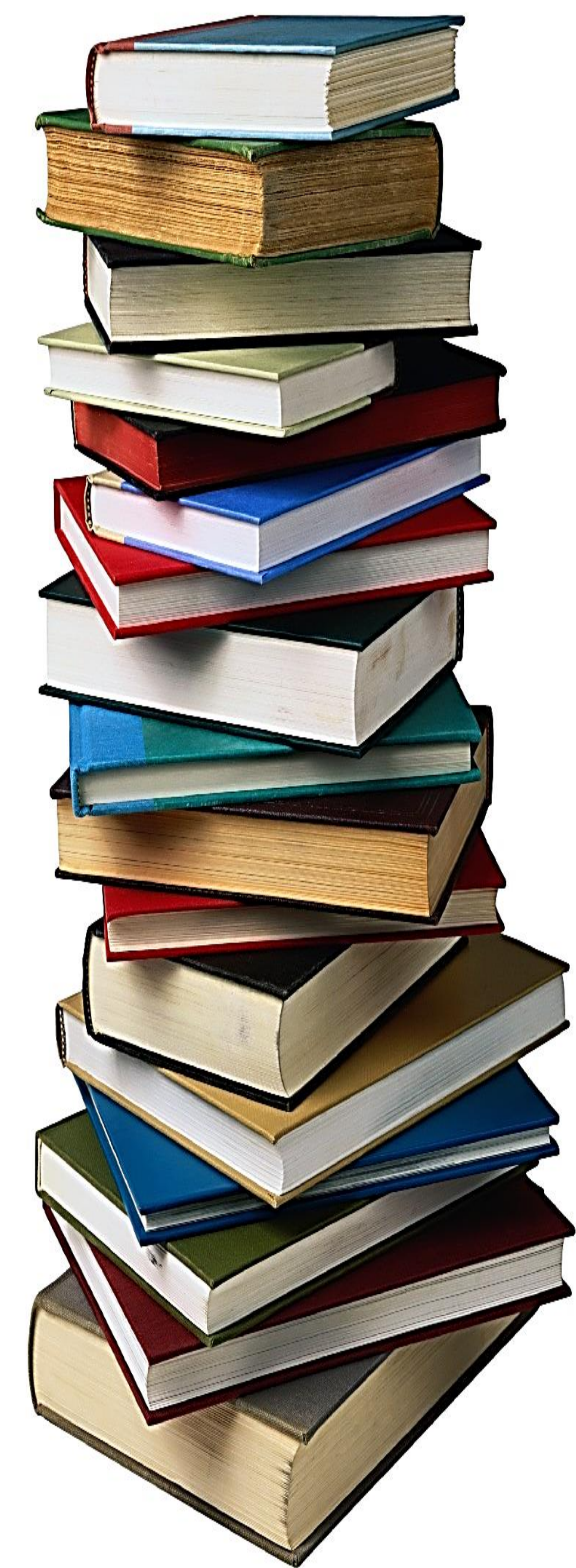
# THE PURPOSE OF THIS PROJECT

This Guide is designed to translate scientific evidence available for probiotic supplements to practical, clinically relevant information, enabling clinicians to easily select the appropriate product, dose, and format for a specific indication.



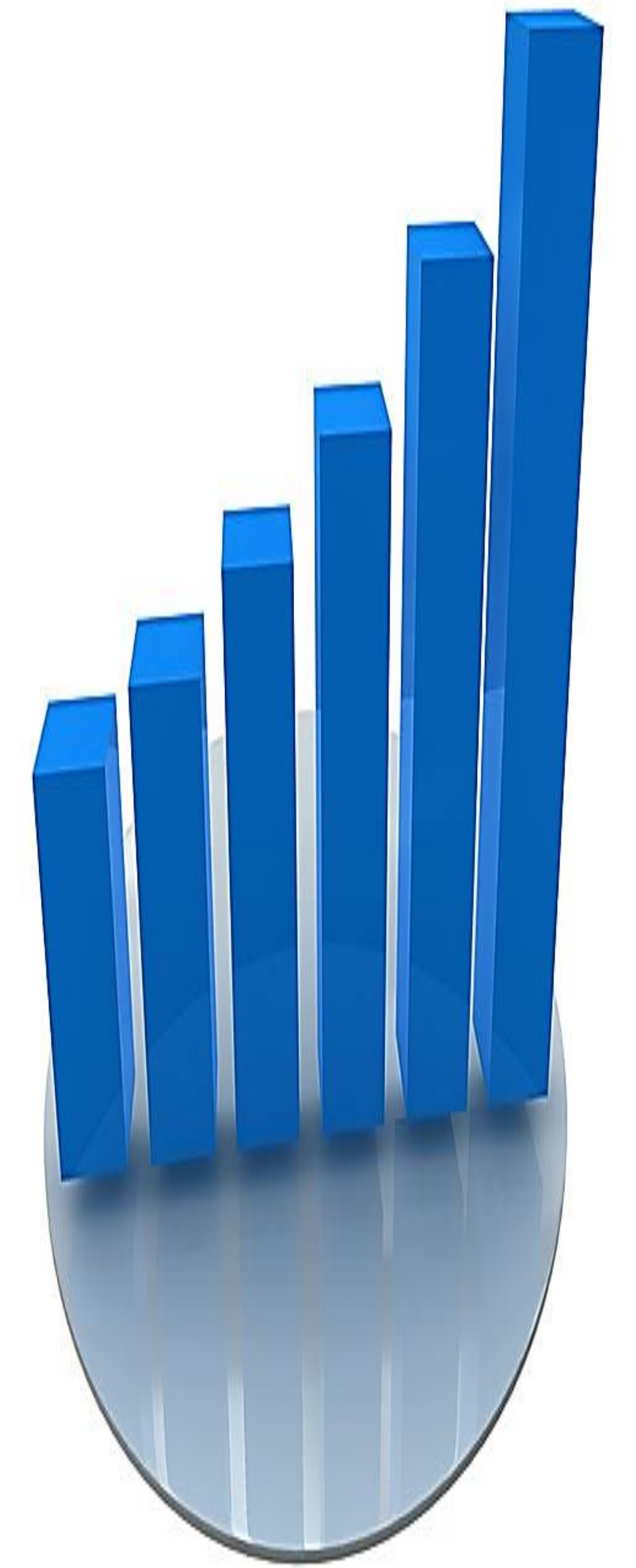
# THE HISTORY OF THE PROJECT

- Project started in 2008 when a gap in translating knowledge on probiotic supplements was identified
- The first version of the Clinical Guide was reviewed and distributed to primary care physicians and allied health care professionals in Canada in 2009.
- This document is updated annually for new products, indications, and evidence, with the Expert Advisory Board of reviewers expanding as well to include a variety of specializations.



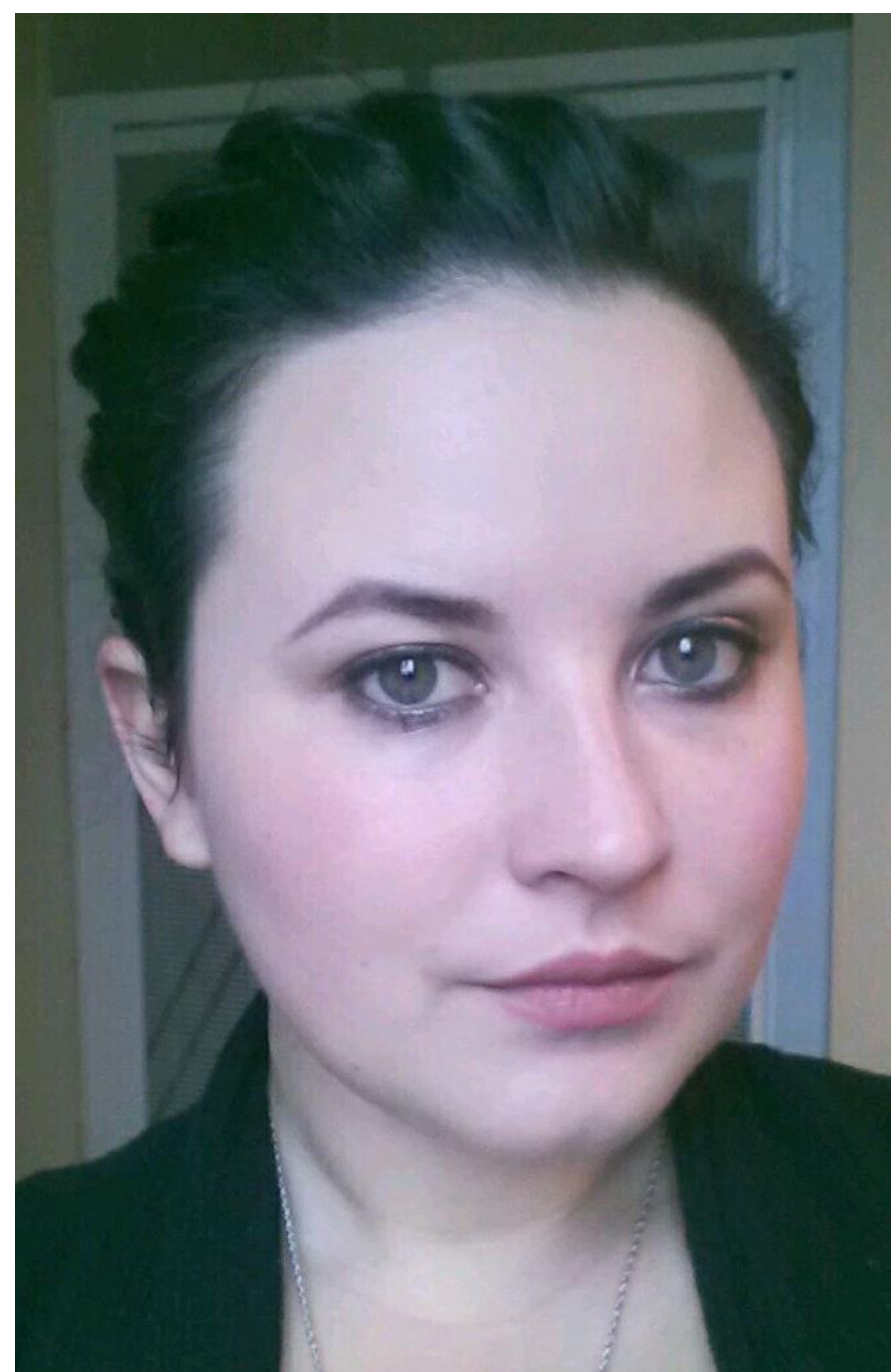
# METHODS

- Published data/ studies with defined clinical outcome for probiotic strain(s) was searched, using inclusion criteria as listed on the Guide
- Commercially available products containing said strain(s) were identified
- The inclusion criteria was used to evaluate the strength of the recommendation for each product.
- Once this information was compiled into a comprehensive chart form, it was assessed by independent expert reviewers.



# MEET THE TEAM BEHIND THE CLINICAL GUIDE:

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Pharmacist Health Educator  
Consultant to Primary Care Family Health Team Action Group as appointed by the Ontario Ministry of Health



# INCLUSION CRITERIA:

1. Commercially available in Canada as a supplement or probiotic-containing functional food
2. Approved by Health Canada (NPN) for probiotic supplements (tablets, capsules, sachets)
3. Published clinical evidence for the particular strain(s) present in each product/food



## Note:

- For products containing multiple strains, evidence must be for the specific combination and not for the separate probiotic strains
- Some products are excluded from the current edition due to changes in the strains used

## ACRONYMS /INDICATIONS

<b>AAD</b>	Antibiotic associated diarrhea - Prevention	<b>BG</b>	Reduces blood glucose in Type II Diabetes (FBG and HA1c)	<b>C</b>	Constipation	<b>CDAD</b>	<i>Clostridium difficile</i> associated diarrhea - Prevention
<b>CD-PP</b>	<i>Clostridium difficile</i> associated diarrhea - Primary prevention	<b>CE/AE</b>	Childhood eczema / Atopic dermatitis	<b>CID</b>	Common infectious disease	<b>FAP</b>	Functional abdominal pain
<b>HP</b>	<i>Helicobacter pylori</i> - Adjunct to standard eradication therapy	<b>ID</b>	Infectious diarrhea	<b>IBD-P</b>	Inflammatory bowel disease - Pouchitis	<b>IBD-UC</b>	IBD - Ulcerative colitis - Adjunct to standard therapy
<b>IBS</b>	Irritable bowel syndrome	<b>LDL-C</b>	Reduces LDL and total cholesterol	<b>NEC*</b>	Necrotizing Enterocolitis (newborn) *as per hospital protocol, not for self-administration	<b>NI</b>	Nosocomial infections prevention
<b>PD</b>	Periodontal disease	<b>Regurg/ GI Mot</b>	Reduces regurgitation/ Improves gastrointestinal motility	<b>TD</b>	Traveler's diarrhea	<b>CFU</b>	Colony forming units (number of viable bacteria)

# LEVELS OF EVIDENCE:

- **Level I: (HIGHEST LEVEL)**
  - Evidence obtained from at least one properly designed randomized trial.
- **Level II:**
  - Evidence obtained from well-designed controlled trials without randomization/
  - Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group/
  - Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.
- **Level III:**
  - Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

# INDICATIONS FOR ADULT HEALTH

Brand Name	Probiotic Strain (s)	Dosage Form	CFU/dose	No. of doses/day	ID	AAD	CDAD	CD-PP	TD	C	IBS	IBD-UC	IBD-P	HP	PD	LDL-C	CID
Align™	<i>B. longum infantis</i> 35624	Capsules	1B/capsule	1 capsule							<sup>1-3</sup>						
BioGaia® drops* BioGaia® chew tabs	<i>L. reuteri protectis</i> DSM 17938	Drops Chew. tabs	100M/5drops 100M/tab	5 drops 1 tab	<sup>4</sup>	<sup>5</sup>								<sup>6-9</sup>			
Bio-K+ CL1285*	<i>L. acidophilus</i> CL 1285 <i>L. casei</i> LBC80R <i>L. rhamnosus</i> CLR2	Regular Capsule Strong Capsule “Travel Protection” Extra Strength	12.5B/capsule 25B/capsule 30B/capsule 50B/capsule	1-2 capsules			<sup>10-12</sup>	<sup>11,13 a</sup>	<sup>13,14 a</sup>								
		Ferm. milk lq. Ferm. rice lq. Ferm, soy lq	50B/tub	½ -1 tub													
Cardioviva™	<i>L. reuteri</i> NCIMB 30242	Capsule	2B/capsule	2 capsules												<sup>15-17</sup>	
Culturelle®	<i>L. rhamnosus</i> GG	Capsule	10B/capsule	1 capsule		<sup>18</sup>								<sup>19</sup>			
Florastor®	<i>Saccharomyces boulardii</i> Iyo	Capsule Sachet	5B/capsule 5B/sachet	1-2 capsules 1-2 sachets		<sup>20, 21</sup>	<sup>13, 21, 22</sup>	<sup>13, 14</sup>	<sup>23-25</sup>			<sup>26</sup>		<sup>27-29</sup>			
Mutaflor® *	<i>Echerichia coli</i> Nissle 1917	Capsule	2.5- 25B/capsule	1-2 capsules								<sup>30-33</sup>					
PerioBalance™	<i>L. reuteri prodentis</i> (ATCC 55730 and ATCC PTA 5289)	Lozenge	100M each/lozenge	2 lozenges											<sup>34, 35</sup>		
Proxiflor® (formerly Lacidofil)	<i>L. rhamnosus</i> R0011 <i>L. helveticus</i> R0052	Capsule	4B/capsule	1-3 capsules							<sup>36</sup>						
TuZen®	<i>L. plantarum</i> 299v	Capsule	10B/capsule	1-2 capsules		<sup>37</sup>	<sup>38</sup>				<sup>39-41</sup>						
UltraFlora™ Cold Support (formerly Health Defense)	<i>L. plantarum</i> HEAL9 <i>L. paracasei</i> 8700:2	Capsule	0.5B each/capsule	1 capsule													<sup>42,43</sup>
VSL#3® *	• <i>L. acidophilus</i> SD5212 • <i>B longum</i> SD5219 • <i>L. casei</i> SD5218 • <i>B. infantis</i> SD5220 • <i>L. bulgaricus</i> SD5210 • <i>B. breve</i> SD5206 • <i>S. thermophilus</i> SD5207 • <i>L. plantarum</i> SD5209	Sachet	450B/sachet	1-4 sachets						<sup>44</sup>		<sup>45-47</sup>	<sup>46, 48-50</sup>				

a. Health Canada, Dec 2012 approved claim for Bio-K+100 (NPN 80038453) : “Helps to reduce the risk of Clostridium Difficile Associated Diarrhea (CDAD) in hospitalized patients”

## INDICATIONS FOR PEDIATRIC HEALTH

Brand Name	Probiotic Strain (s)	Dosage Form	CFU/dose	No. doses /day	Regurg/ GI Mot	NEC* (newborn)	Colic	ID	AAD	CDAD	IBD-UC	HP	C	IBS/FAP	CID	NI	CE/AD	
BioGaia® drops* BioGaia® chew tabs	<i>L. reuteri protectis</i> DSM 17938	Drops Chew. tabs	100M/5drops 100M/tab	5 drops 1 tab	51,52,53* Preterm infants *full term infants	54	55-58	59-63	64				65,66	67,68	69,70		71	
Culturelle®	<i>L. rhamnosus</i> GG	Powder	1B/packet	6-10 packets				72-77	78,79					80,81		82* *> 12yo	83-89	
FloraBABY *	• <i>B. breve</i> HA-129 1.2B • <i>L. rhamnosus</i> HA-111 1B • <i>B. bifidum</i> HA-132 0.8B • <i>B. infantis</i> HA-116 0.6B • <i>B. longum</i> HA-135 0.4B	Powder	4B/scoop	1 scoop		90												
Florastor®	<i>Saccharomyces boulardii</i> lyo	Capsule Sachet	5B/capsule 5B/sachet	1-2 capsules 1-2 sachets				91-93	94	95		28						
Junior Daily Probiotic (formerly DDS® Junior)	<i>B. lactis</i> UABLA-12 4.2B <i>L. acidophilus</i> DDS®-1 0.8B	Powder	5B/gram	2 grams												96	97	
Proxiflor® (formerly Lacidofil)	<i>L. rhamnosus</i> R0011 3.8B <i>L. helveticus</i> R0052 0.2B	Capsule	4B/capsule	1 capsule													98	
UltraFlora™ Children's	<i>L. acidophilus</i> NCFM® <i>B. animalis subsp lactis</i> Bi-07	Chewable tablet	2.5B each/chewable tablet	1-2 chew. tablets												99		
VSL#3*	• <i>L. acidophilus</i> SD5212 • <i>L. casei</i> SD5218 • <i>L. bulgaricus</i> SD5210 • <i>L. plantarum</i> SD5209 • <i>B. longum</i> SD5219 • <i>B. infantis</i> SD5220 • <i>B. breve</i> SD5206 • <i>S. thermophilus</i> SD5207	Sachet	450B/sachet	1-2 sachets				100				101,102			103			

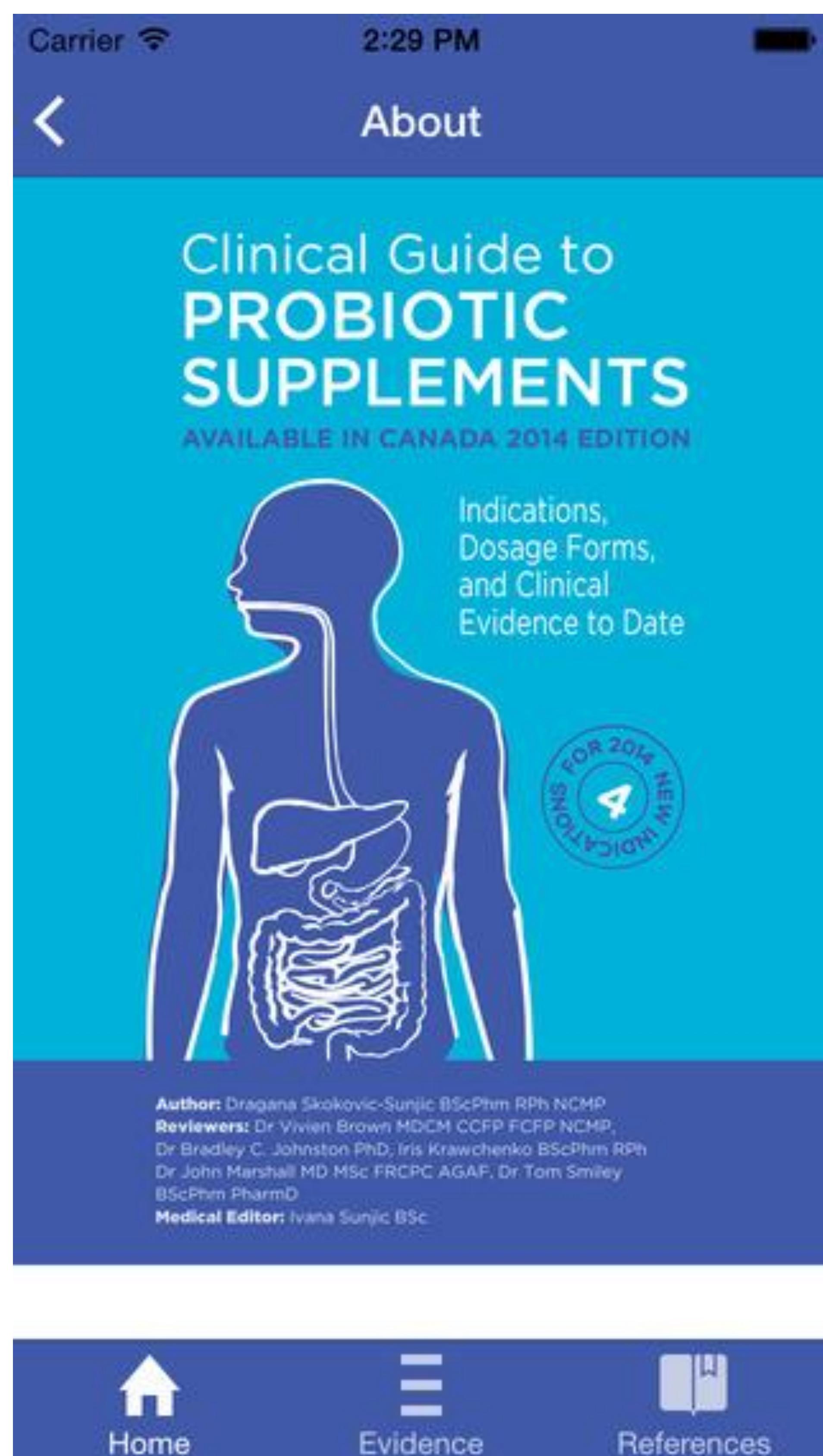
## INDICATIONS FOR VAGINAL HEALTH

Brand Name	Probiotic Strain (s)	Dosage Form	CFU per dose	No. of doses / day	Vulvovaginal candidiasis	Bacterial vaginosis
ProB™ (RePhresh ProB) and Fem-Dophilus®	<i>L. rhamnosus</i> GR-1 <i>L. reuteri</i> RC-14	Oral capsule	2.5B each/capsule	1 capsule	<sup>104,105</sup>	<sup>106-108</sup>
Probaclac BV®	<i>L. acidophilus</i> A-212 0.4B <i>L. rhamnosus</i> A-119 6.8B <i>S. thermophilus</i> A-336 0.8B	Vaginal capsule	8B/capsule	1-2 capsules		<sup>109</sup>
Provacare™	<i>L. rhamnosus</i> Lcr35	Vaginal capsule	3.41B/capsule	2 capsules	<sup>110</sup>	<sup>111-113</sup>
Purfem™	<i>L. rhamnosus</i> PBO1, <i>L. gasseri</i> EN-153471 (EB01)	Vaginal ovule	1B each/ovule	1 ovule		<sup>114,115</sup>
UltraFlora™ Women's	<i>L. reuteri</i> RC-14 <i>L. rhamnosus</i> GR-1	Oral capsule	1B each/capsule	2 capsules	<sup>116</sup>	<sup>117,118</sup>

## FUNCTIONAL FOODS WITH ADDED PROBIOTICS

Brand Name	Probiotic Strain (s)	Dosage Form (CFU) At the time of packaging	No. of doses / day	Children				Adults				
				ID	HP	AAD	CID	AAD	IBS	HP	C	BG
Activia® ❄️	<i>B. lactis</i> CNCM I-2494 (formerly DN-173 010)	1B/serving	1-3 servings						<sup>119,120</sup>		<sup>121</sup>	
DanActive® ❄️	<i>L. casei sp. paracasei</i> CNCM I-1518 (formerly DN-114 001)	10B/serving	1-2 servings	<sup>122-124</sup>	<sup>125</sup>		<sup>126</sup>	<sup>127</sup>				
Nestlé® Gerber® Infant Cereals	<i>B. lactis</i> BB-12 DSM 10140	1B/28 g serving	1 serving			<sup>128,129</sup>	<sup>128,129</sup>					
Nestlé® Gerber® Toddler Cereals		1B/35 g serving	1 serving			<sup>128,129</sup>	<sup>128,129</sup>					
Nestlé® Gerber® Graduates Toddler Drink		1B/200mL serving	1 serving			<sup>128,129</sup>	<sup>128,129</sup>					
Nestlé® Good Start® Probiotic Infant Formula		130 M/100mL serving	Routine feeding if an alternative to breast milk is required			<sup>130</sup>						
Yoptimal® ❄️ and iOGO Probio™ ❄️	<i>B. lactis</i> BB-12 <i>L. acidophilus</i> LA-5	1B/100g	1-3 servings							<sup>131-134</sup>	<sup>135,136</sup>	<sup>137</sup>

# Thanks to support by AEP members (Alliance for Education in Probiotic)



Clinical Guide is available online at:  
**[www.probioticguide.ca](http://www.probioticguide.ca)**



Available as **PROBIOTIC** mobile app





# CONCLUSIONS

- ✓ There is an emerging role of probiotics in prevention and treatment
- ✓ Not all probiotics are created equal or offer the same level of clinical evidence

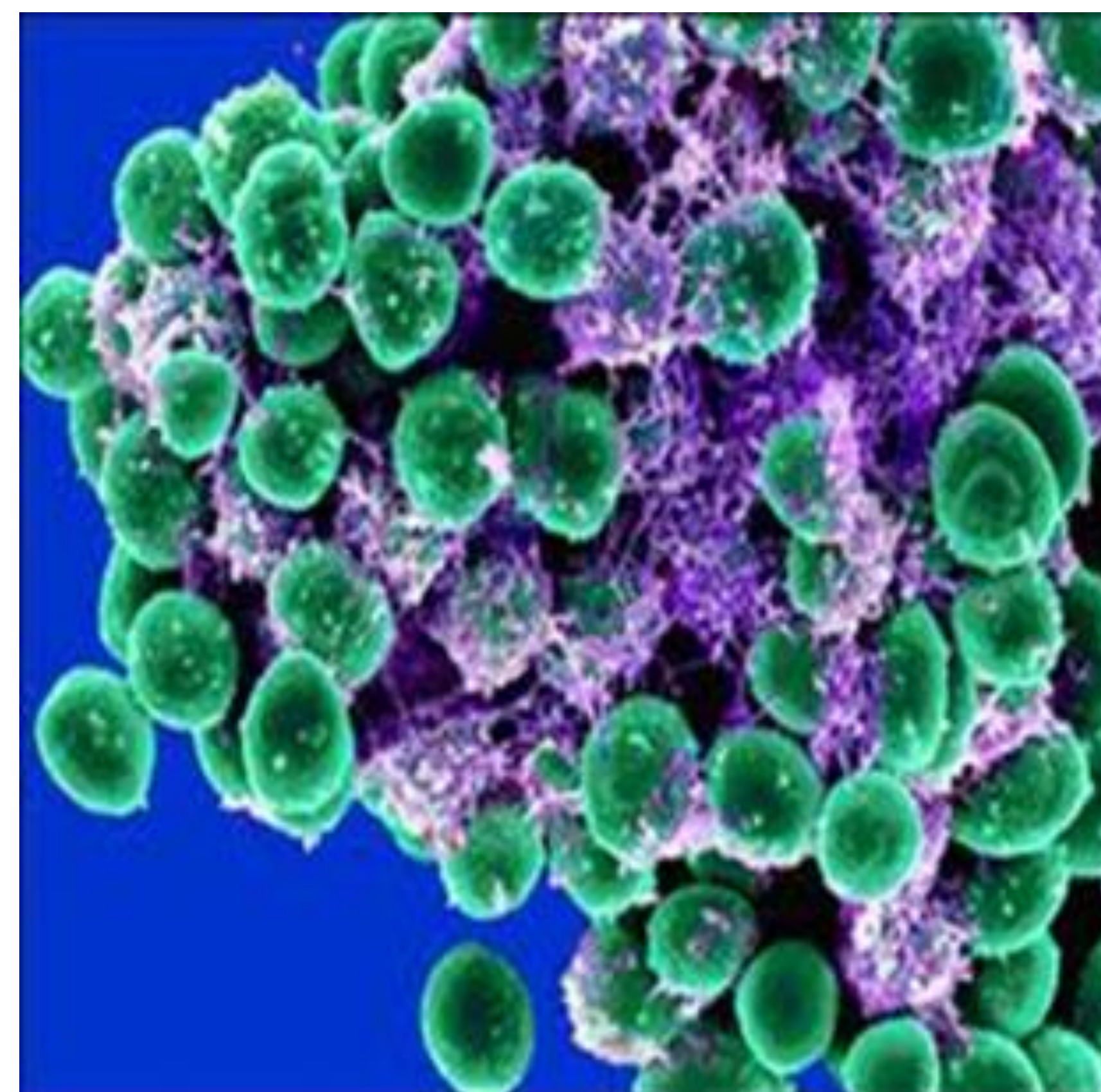


Photo: Microsoft clipart

# PRACTICE PEARLS

Recommendation should be based on:

- ✓ Demonstrated **efficacy** for specific **indication**
- ✓ Defined **strain** of bacteria
- ✓ Correct **dose** for a specific condition
- ✓ **Quality product** that abides by the principles of Good Manufacturing Processes

# THANK YOU



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