SEE PAIN RELIEF PLACED DIRECTLY AT THE SOURCE OF PAIN

XARACOLL

The **FIRST** and **ONLY** implant to deliver local, long-lasting, postsurgical analgesia for up to 24 hours following **OPEN INGUINAL HERNIA REPAIR** in adults

INDICATIONS AND USAGE

XARACOLL is indicated in adults for placement into the surgical site to produce postsurgical local analgesia for up to 24 hours following open inguinal hernia repair.

Limitations of Use: Safety and effectiveness have not been established in other surgical procedures, including orthopedic and boney procedures.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Most common adverse reactions in clinical trials (incidence ≥2% and higher than placebo) included incision site swelling, dysgeusia, headache, tremor, blurred vision, seroma, scrotal swelling, pyrexia, oral hypoaesthesia, and post procedural discharge.

Please see complete Important Safety Information on last page and accompanying full Prescribing Information.

xaracoll®
(bupivacaine HCl) implant

SEE

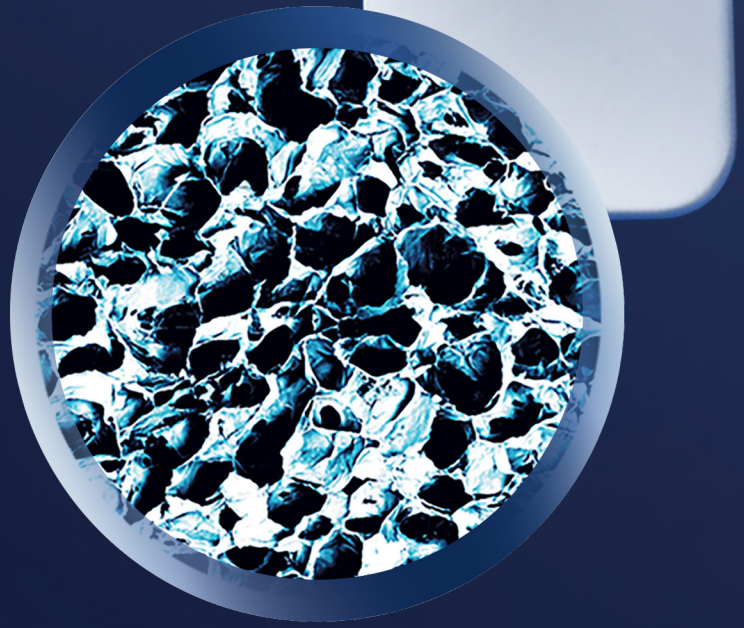
A LOCAL APPROACH TO POSTSURGICAL

PAIN RELIEF

A fully resorbable bovine collagen implant containing bupivacaine HCl manufactured with a proprietary process offering surgeon and patient benefits

Actual Implant Size:
5 cm x 5 cm x 0.5 cm

Magnification: 200X[1]



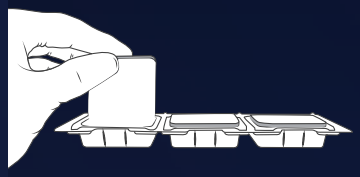
- Designed as a ready-to-use product requiring no special preparation
- Collapses, conforms, and stays in place when placed at the surgical site[1]
- Releases bupivacaine immediately and over time[1,2]
  - In a 52-patient pharmacokinetics (PK) study, local placement of XARACOLL resulted in detectable plasma levels of bupivacaine at the first measured time point (0.5 hours) and throughout the 96-hour observation period.[2] Systemic plasma levels of bupivacaine following application of XARACOLL do not correlate with local efficacy
  - In vitro dissolution study results showed bupivacaine release as quickly as 5 minutes and through 24 hours[1]
- The toxic effects of local anesthetics are additive. Avoid additional local anesthetic administration within 96 hours following XARACOLL implantation. If additional local anesthetic administration with XARACOLL cannot be avoided, monitor patients for neurologic and cardiovascular effects related to local anesthetic systemic toxicity

xaracoll®
(bupivacaine HCl) implant

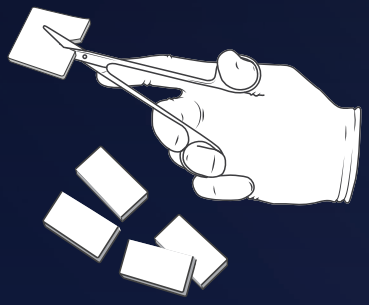
PAIN RELIEF YOU CAN SEE PLACED AT THE SOURCE OF PAIN

Three fully resorbable collagen implants, each containing 100 mg bupivacaine HCl, for a total dose of 300 mg

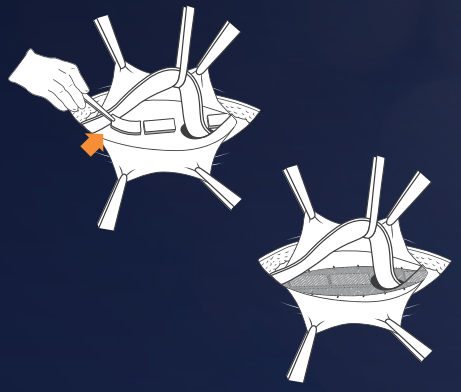
Intended for single-dose administration. Please see full placement instructions in Prescribing Information.



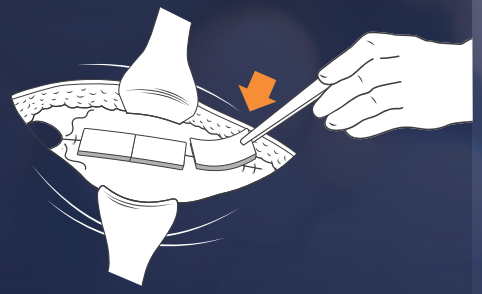
From package to procedure with no need for special preparation



3 collagen implants should be cut in half and placed into surgical site dry



3 halves should be placed into the inguinal hernia repair site below the site of mesh placement



3 remaining halves should be placed between the muscle/fascia layer and skin closure

ADDITIONAL PLACEMENT INSTRUCTIONS

- Supplied as a sterile product that should be handled using aseptic technique
- Inspect packaging and implants; do not use if damaged
- Outer pouch and inner blister should be peeled open aseptically
- Avoid excessive handling and compression of the collagen implants

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Known hypersensitivity to bupivacaine or to any local anesthetic agent of the amide-type or to other components of XARACOLL
- Obstetrical paracervical block anesthesia. The use of bupivacaine in this technique has resulted in fetal bradycardia and death

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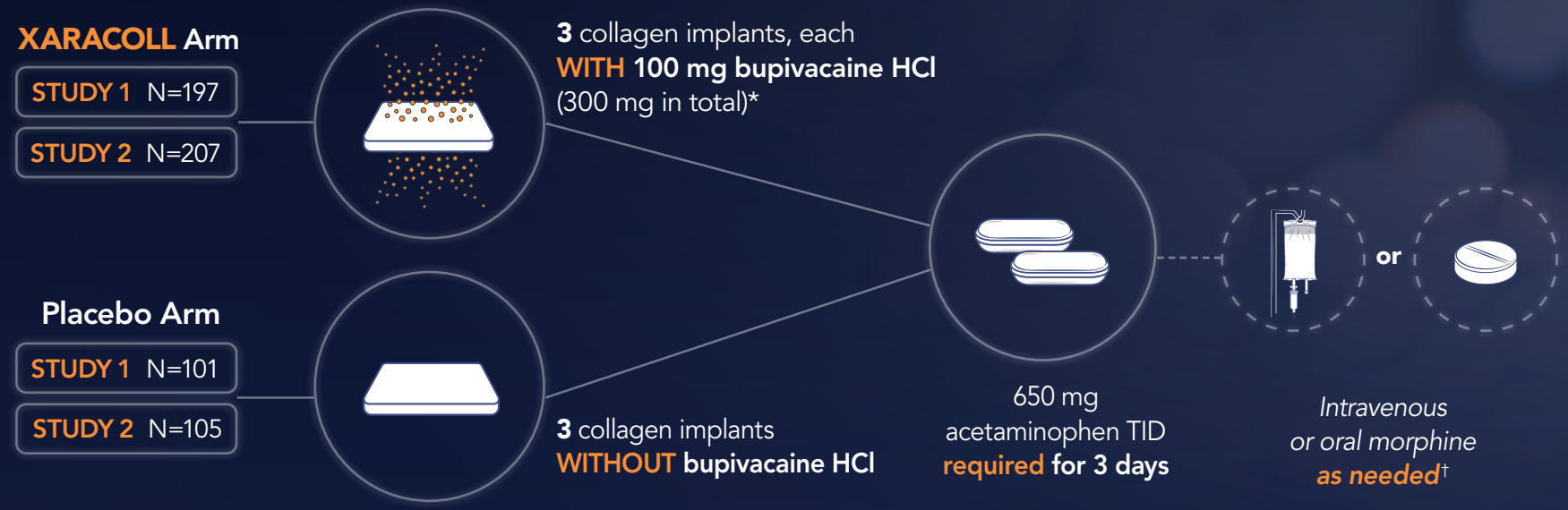
(bupivacaine HCl) implant

TWO PHASE III STUDIES IN OPEN INGUINAL HERNIOPLASTY

Two Phase III studies of identical design were performed as outpatient surgeries in adults across 39 sites in the US[1]

PATIENT RANDOMIZATION ACROSS BOTH STUDIES (N=610)



PRIMARY ENDPOINT: Time-weighted sum of pain intensity from 0 through 24 hours‡

SECONDARY ENDPOINT: Total use of opioid analgesia (TOpA)

*Doses above 300 mg per patient have not been studied in clinical trials. †Intravenous morphine provided until patients were able to tolerate oral morphine. ‡Sum of Pain Intensity is an FDA-accepted measurement of pain, calculated by using patient ratings of pain intensity on a 0-10 scale reported at multiple points from baseline over a time period.[3]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Dose-Related Toxicity:** Monitor cardiovascular and respiratory vital signs and patient's state of consciousness after placement of XARACOLL
- **Methemoglobinemia:** Cases of methemoglobinemia have been reported in association with local anesthetic use. See full Prescribing Information for more detail on managing these risks

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SIGNIFICANT PAIN RELIEF YOU CAN SEE THROUGH 24 HOURS

STUDY 1

XARACOLL patients had a 20% reduction in pain and used 50% fewer opioids vs placebo[3]

20%

MEAN REDUCTION IN PAIN INTENSITY*

XARACOLL	85.9
Placebo	106.8
P Value	0.0004

50%

LESS OPIOID USE†

XARACOLL	5 mg
Placebo	10 mg
P Value	<0.0001

STUDY 2

XARACOLL patients had a 24% reduction in pain and used 64% fewer opioids vs placebo[3]

24%

MEAN REDUCTION IN PAIN INTENSITY*

XARACOLL	88.3
Placebo	116.2
P Value	<0.0001

64%

LESS OPIOID USE†

XARACOLL	5 mg
Placebo	14 mg
P Value	<0.0001

*Primary endpoint.

†Median IV morphine mg equivalent.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- Known hypersensitivity to bupivacaine or to any local anesthetic agent of the amide-type or to other components of XARACOLL
- Obstetrical paracervical block anesthesia. The use of bupivacaine in this technique has resulted in fetal bradycardia and death

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DATA THROUGH 48 HOURS

STUDY 1: Did not achieve statistical significance of *P*=0.05 vs placebo.[3]

XARACOLL patients had an 11% reduction in pain and used 64% fewer opioids vs placebo[3]

11%

MEAN REDUCTION IN PAIN INTENSITY

XARACOLL	**179.3**
Placebo	201.3
P Value	0.0568

64%

LESS OPIOID USE*

XARACOLL	5 mg
Placebo	14 mg
P Value	—

STUDY 2

XARACOLL patients had an 11% reduction in pain and used 50% fewer opioids vs placebo[3]

11%

MEAN REDUCTION IN PAIN INTENSITY

XARACOLL	**192.6**
Placebo	216.8
P Value	0.0270

50%

LESS OPIOID USE*

XARACOLL	10 mg
Placebo	20 mg
P Value	0.0003

*Median IV morphine mg equivalent.

IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS

Local Anesthetics: The toxic effects of local anesthetics are additive. Avoid additional local anesthetic administration within 96 hours following XARACOLL implantation. If additional local anesthetic administration with XARACOLL cannot be avoided, monitor patients for neurologic and cardiovascular effects related to local anesthetic systemic toxicity.

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PATIENTS REQUIRING NO OPIOIDS FROM 0 TO 72 HOURS

In two clinical studies, up to 36% of XARACOLL patients did not need opioids through 72 hours[3]*

STUDY 1

Patients NOT USING Opioids (%)

36% XARACOLL

22% Placebo

STUDY 2

Patients NOT USING Opioids (%)

28% XARACOLL

12% Placebo

*There was no statistically significant treatment effect for XARACOLL compared to placebo in SPI72 and TOpA72.

WARNINGS AND PRECAUTIONS

- **Dose-Related Toxicity:** Monitor cardiovascular and respiratory vital signs and patient's state of consciousness after placement of XARACOLL
- **Methemoglobinemia:** Cases of methemoglobinemia have been reported in association with local anesthetic use. See full Prescribing Information for more detail on managing these risks

IMPORTANT SAFETY INFORMATION

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Based on animal data, may cause fetal harm
- **Moderate to Severe Hepatic Impairment:** Consider increased monitoring for bupivacaine systemic toxicity

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SAFETY PROFILE IN PHASE III STUDIES

Adverse reactions with incidence ≥2% and greater than placebo

	XARACOLL (N=411) n (%)	Placebo* (N=208) n (%)
Subjects Reporting Treatment Emergent Adverse Events	**256 (62.3)**	**143 (68.8)**
Injury, Poisoning, and Procedural Complications		
Incision site swelling	60 (14.6)	30 (14.4)
Post procedural discharge	20 (4.9)	10 (4.8)
Seroma	12 (2.9)	5 (2.4)
Nervous System Disorders		
Dysgeusia	31 (7.5)	13 (6.3)
Headache	17 (4.1)	1 (0.5)
Tremor	15 (3.6)	6 (2.9)
Gastrointestinal Disorders		
Hypoaesthesia oral	9 (2.2)	4 (1.9)
Reproductive System and Breast Disorders		
Scrotal swelling	12 (2.9)	2 (1.0)
General Disorders and Administration Site Conditions		
Pyrexia	10 (2.4)	1 (0.5)
Eye Disorders		
Vision blurred	15 (3.6)	6 (2.9)

*Placebo consisted of three collagen implants.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Most common adverse reactions in clinical trials (incidence ≥2% and higher than placebo) included incision site swelling, dysgeusia, headache, tremor, blurred vision, seroma, scrotal swelling, pyrexia, oral hypoaesthesia, and post procedural discharge.

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SAFETY PROFILE IN PHASE III STUDIES

- **In Phase III clinical studies, eight patients reported serious adverse events (SAEs), none of which was considered treatment related[3]**
- Five patients (1.2%) receiving XARACOLL reported 15 SAEs in 5 system organ classes[1]
  - Cardiac
  - Gastrointestinal
  - Infections/infestations
  - Metabolism/nutrition
  - Renal/urinary disorders
- Three patients (1.4%) receiving placebo reported 3 SAEs in 3 system organ classes[1]
  - Cardiac (1 fatal)
  - Gastrointestinal
  - Musculoskeletal/connective tissue disorders

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

Most common adverse reactions in clinical trials (incidence ≥2% and higher than placebo) included incision site swelling, dysgeusia, headache, tremor, blurred vision, seroma, scrotal swelling, pyrexia, oral hypoaesthesia, and post procedural discharge.

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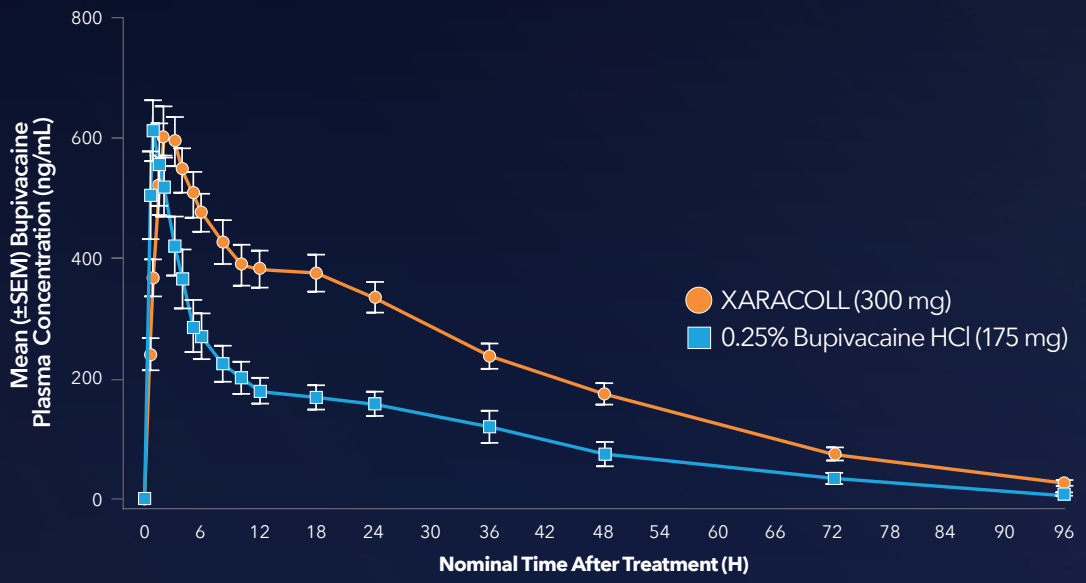
PHARMACOKINETICS

PK Study Design: A multicenter, randomized, single-blind, active comparator-controlled study. 52 patients were randomized prior to open inguinal hernioplasty in a 2:1 ratio to receive either 3 x 100 mg XARACOLL bupivacaine HCl collagen implants (total bupivacaine HCl dose 300 mg) or Marcaine® 0.25% (bupivacaine HCl) 175-mg infiltration.[2]

The most common treatment-related adverse events reported, experienced by patients across treatments, were tremors (8.8% vs 6.3%), dysgeusia (5.9% vs 6.3%), and somnolence (5.9% vs 6.3%), for patients receiving XARACOLL vs placebo, respectively.[2]



Delivers bupivacaine immediately and over time

In a 52-patient pharmacokinetics (PK) study, local placement of XARACOLL resulted in detectable plasma levels of bupivacaine at the first measured time point (0.5 hours) and throughout the 96-hour observation period.[2] Systemic plasma levels of bupivacaine following application of XARACOLL do not correlate with local efficacy.

Marcaine is a registered trademark of Hospira, Inc.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Dose-Related Toxicity:** Monitor cardiovascular and respiratory vital signs and patient's state of consciousness after placement of XARACOLL

xaracoll® (bupivacaine HCl) implant

SEE PAIN RELIEF PLACED DIRECTLY AT THE SOURCE OF PAIN

- Simple implant placement into the surgical site
- Proven, long-lasting pain relief[3]
- Significant reduction in opioid use[3]
- Most common adverse reactions in clinical trials included incision site swelling, dysgeusia, headache, tremor, blurred vision, seroma, scrotal swelling, pyrexia, oral hypoaesthesia, and post procedural discharge

INDICATIONS AND USAGE

XARACOLL is indicated in adults for placement into the surgical site to produce postsurgical local analgesia for up to 24 hours following open inguinal hernia repair.

Limitations of Use

Safety and effectiveness have not been established in other surgical procedures, including orthopedic and boney procedures.

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ORDERING XARACOLL

INDICATION	XARACOLL is indicated in adults for placement into the surgical site to produce postsurgical local analgesia for up to 24 hours following open inguinal hernia repair.
NDC NUMBERS	**4 units:** 51715-100-04 **10 units:** 51715-100-10
HOW SUPPLIED	XARACOLL (bupivacaine HCl) implant is supplied as three white to off-white sterile surgical implants (approximately 5 cm × 5 cm × 0.5 cm), each containing 100 mg bupivacaine HCl in individually sealed blister packages. A tray of three blister packages in a sterile pouch is provided in one carton. XARACOLL is available as: • **Four single-use cartons**, each containing one pouch containing 3 x 100 mg implants (NDC 51715-100-04) • **Ten single-use cartons,** each containing one pouch containing 3 x 100 mg implants (NDC 51715-100-10)
DIMENSIONS OF BOX (LxWxH)	Each unit carton is 170 mm x 25 mm x 287 mm **4-unit case:** 173 mm x 106 mm x 290 mm **10-unit case:** 260 mm x 173 mm x 290 mm
ORDERING	XARACOLL can be ordered using standard ordering procedures through your wholesaler for next-day delivery. • **AmerisourceBergen Corporation: (844) 222-2273** • **Cardinal Health: (800) 926-3161** • **Cardinal Health Specialty Distribution: (866) 677-4844** • **McKesson Customer Support for Hospitals: (855) 625-7385**
STORAGE AND HANDLING	**Storage:** XARACOLL should be stored at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (between 59°F and 86°F). Brief exposure to temperatures up to 40°C (104°F) may be tolerated provided the mean kinetic temperature does not exceed 25°C (77°F); however, such exposure should be minimized. **Handling** prior to surgical placement: • Do not use if pouch or blister packaging has been compromised • Avoid excessive handling • Keep away from moisture • Maintain sterility

$234 per surgery*

*Wholesale Acquisition Cost.

IMPORTANT SAFETY INFORMATION

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(bupivacaine HCl) implant

REFERENCES

1. Data on File. Innocoll Pharmaceuticals Limited.
2. Leiman D, Niebler G, Minkowitz H. Pharmacokinetics and safety of the bupivacaine collagen-matrix implant (INL-001) compared to liquid bupivacaine infiltration after open inguinal hernia repair. Poster presented at: World Congress on Regional Anesthesia & Pain Medicine; April 19-21, 2018; New York, NY. Accessed July 30, 2020. https://epostersonline.com/ASRAWORLD18/node/1154
3. Velanovich V, Rider P, Deck K, et al. Safety and efficacy of bupivacaine HCl collagen-matrix implant (INL-001) in open inguinal hernia repair: results from two randomized controlled trials. *Adv Ther.* 2019;36:200-216.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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To report SUSPECTED ADVERSE REACTIONS, contact Innocoll at 1-833-606-1421 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

DRUG INTERACTIONS

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USE IN SPECIFIC POPULATIONS

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