Heritability and impact of genomics in dairy cattle

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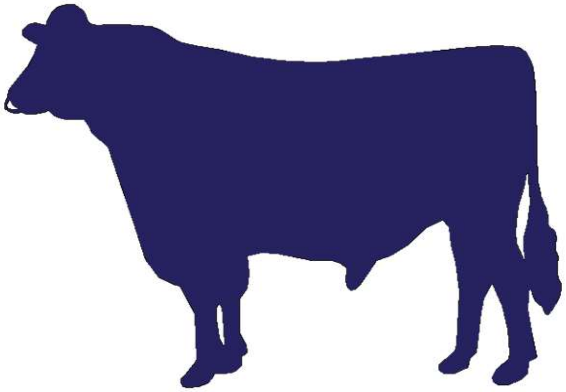
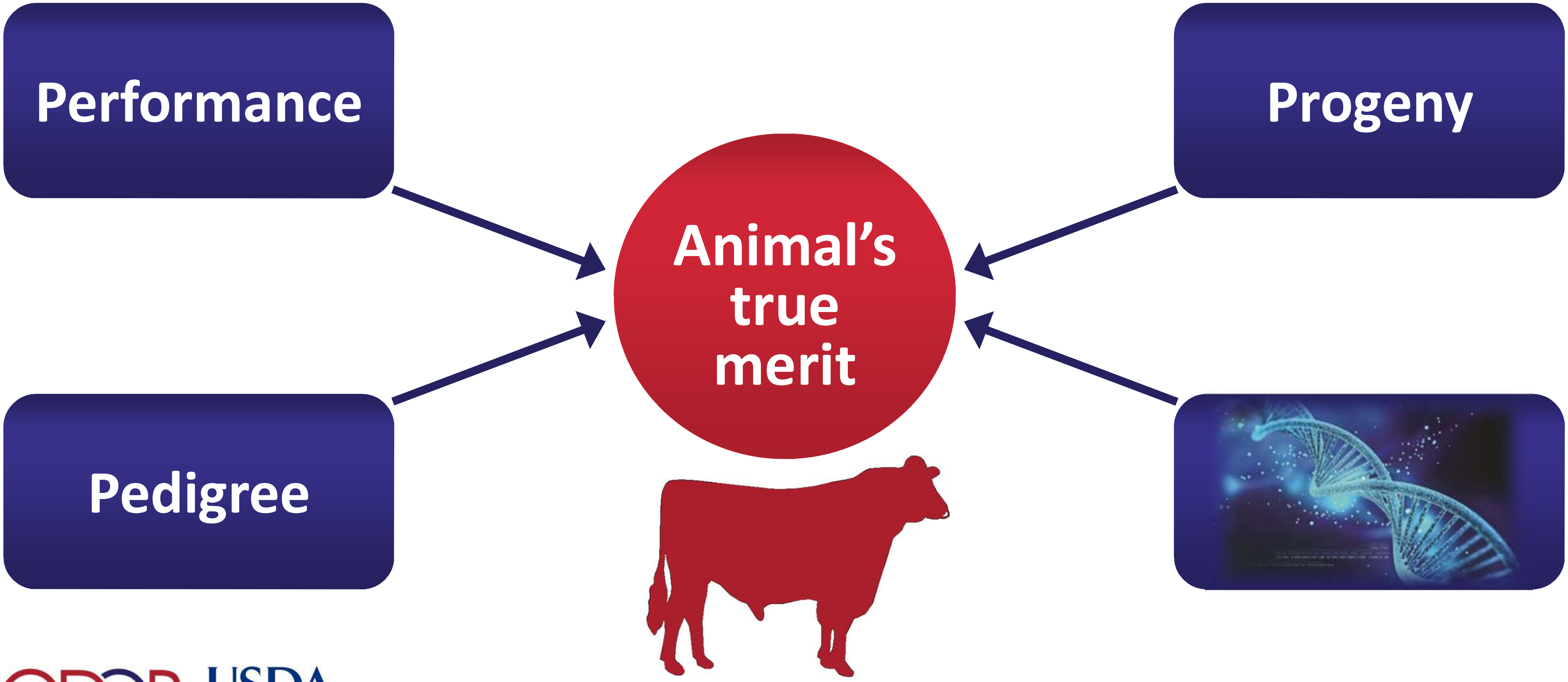
USDA
United States
Department of
Agriculture

Genetic improvement

- Driven by genetic evaluation program
- Yield, fitness, type, and calving traits evaluated
- Widespread use of AI sires
- Intense selection on bulls used in AI
  - Young bulls with genomic evaluations
  - Progeny-tested bulls with daughter records



Adding DNA to the prediction



Performance

Progeny

Animal's true merit

Pedigree

Dairy cattle selection before genomics

- Slow!
  - Progeny test for production took 3–4 years from insemination
  - Bull at least 5 years old before first evaluation available

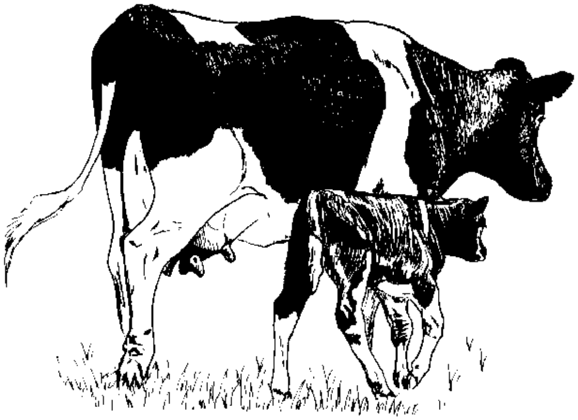
- Expensive!
  - Progeny testing cost $25,000–$50,000 per bull
  - Only 1 in 8–10 bulls graduated from progeny test
  - At least $200,000 invested in each active bull
  - Average active bulls cost about $350,000–$400,000

How do we use genomics

- Identify DNA sequences associated with production traits and disease resistance
- Animals can be evaluated as soon as DNA can be obtained
- Best animals to be parents can now be determined earlier and more accurately

Use of genomic evaluations for AI

- Determine which young bulls to bring into AI
- Use to select mating sires
- Pick bull dams
- Market semen from young bulls



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Highlights of U.S. system

- Nearly 700,000 animals genotyped in 2018
- 69% of AI breedings to genomic bulls
- Genomic relationship between genotyped cows and marketed bulls available to avoid matings giving high inbreeding
- Evaluations on new animals released weekly

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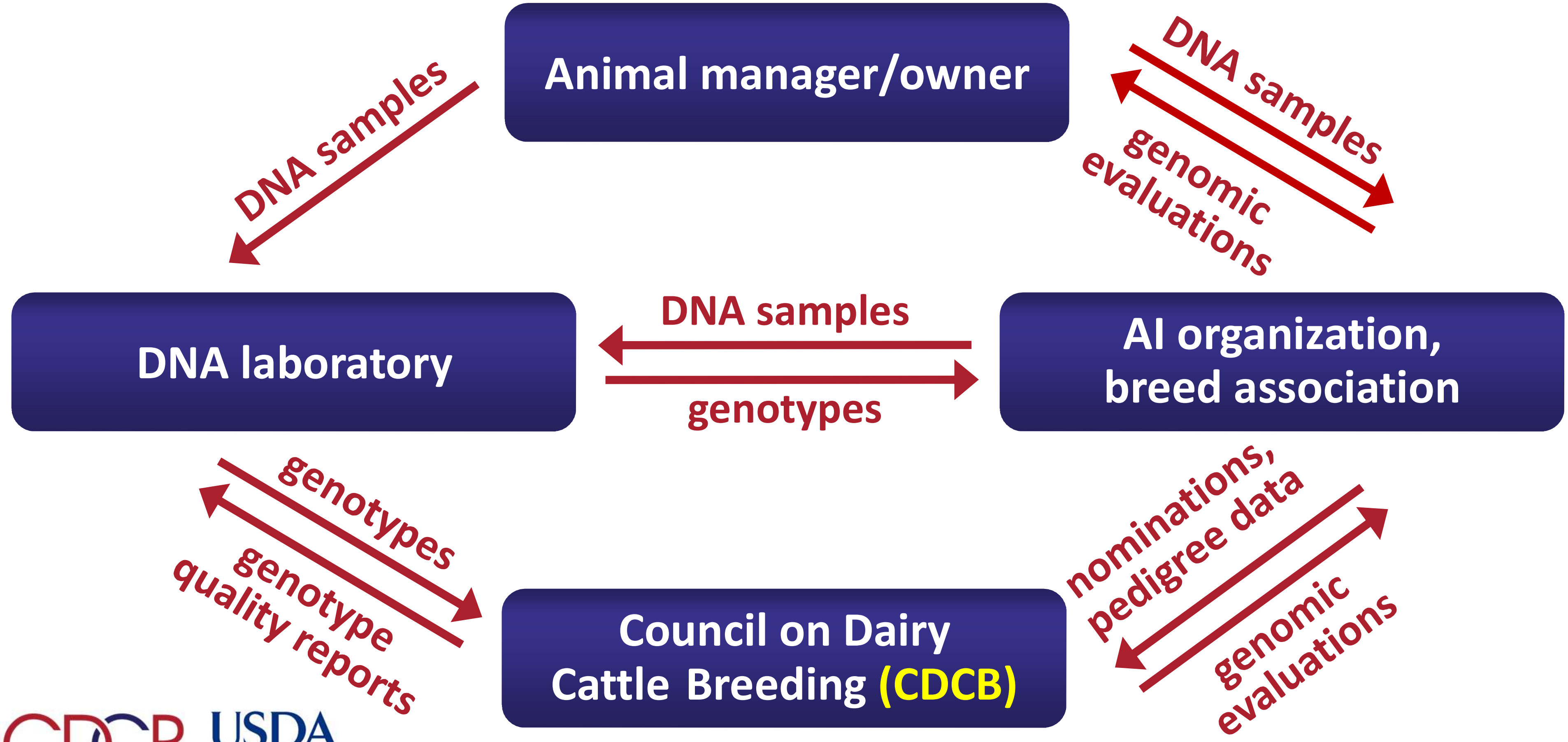
U.S. dairy genomics history

• Dairy DNA repository (Canada, U.S.)	1992
• Cattle genome sequenced	2004
• Illumina 50K SNP BeadChip	2007
• Official genomic evaluations (Holstein, Jersey, Brown Swiss)	2009
• High-reliability, low-density chip	2011
• Genomic evaluations transferred from USDA to CDCB	2013

Genomic data flow



Animal manager/owner

DNA samples

DNA samples

genomic evaluations

DNA laboratory

DNA samples

genotypes

AI organization, breed association

genotypes

genotype quality reports

Council on Dairy Cattle Breeding (CDCB)

nominations, pedigree data

genomic evaluations

DNA Source

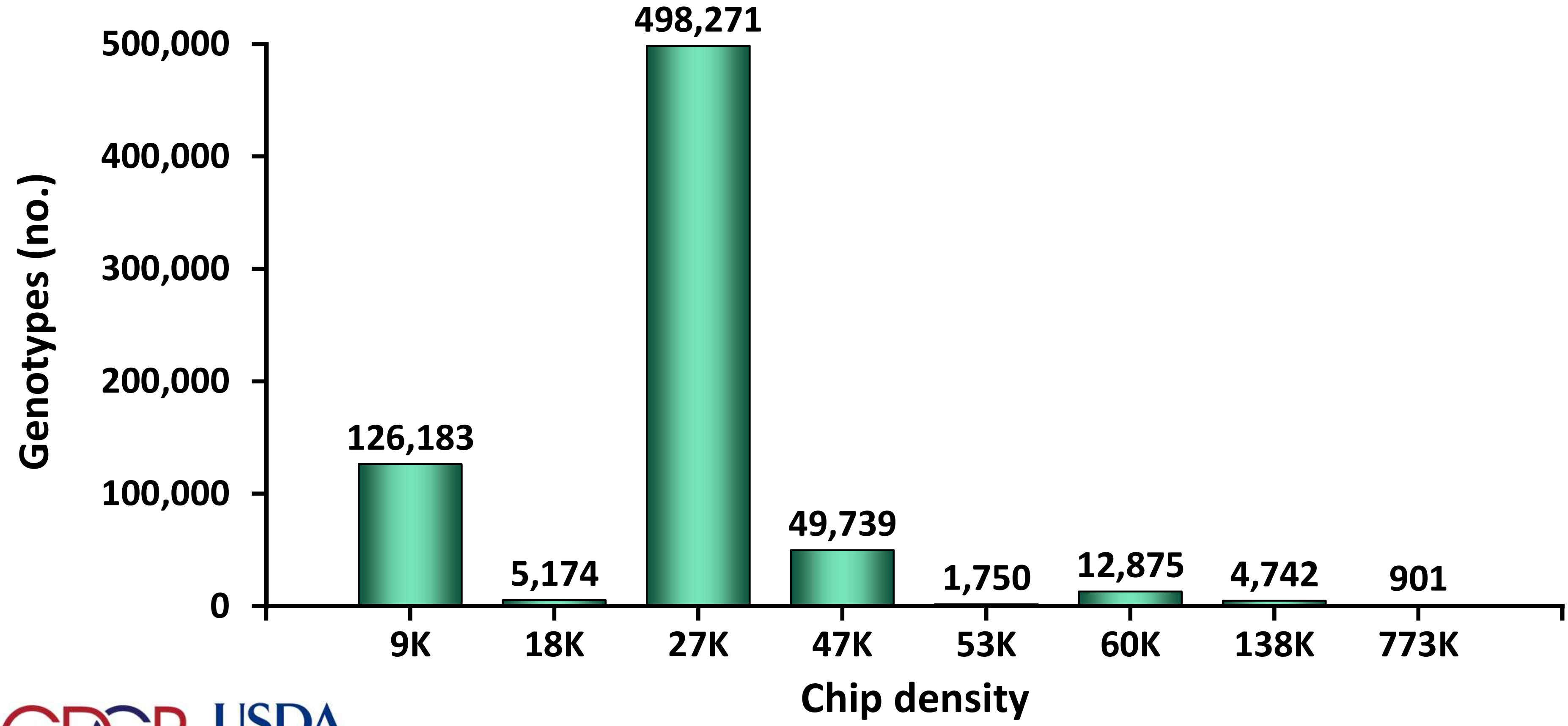
Samples sent to genotyping labs in 2018

Source	Samples (no.)	Samples (%)
Blood	14,656	2
Hair	102,229	14
Nasal swab	656	<1
Semen	319	<1
Tissue	579,255	81
Unknown	17,048	2

Laboratory quality control

- Each SNP evaluated for
    - Call rate
    - Portion heterozygous
    - Parent-progeny conflicts
- Clustering investigated if SNP exceeds limits
- Number of failing SNPs indicates quality of submission
- PASS/FAIL report on 7 conditions sent to labs

Genotype counts by chip density (2018)



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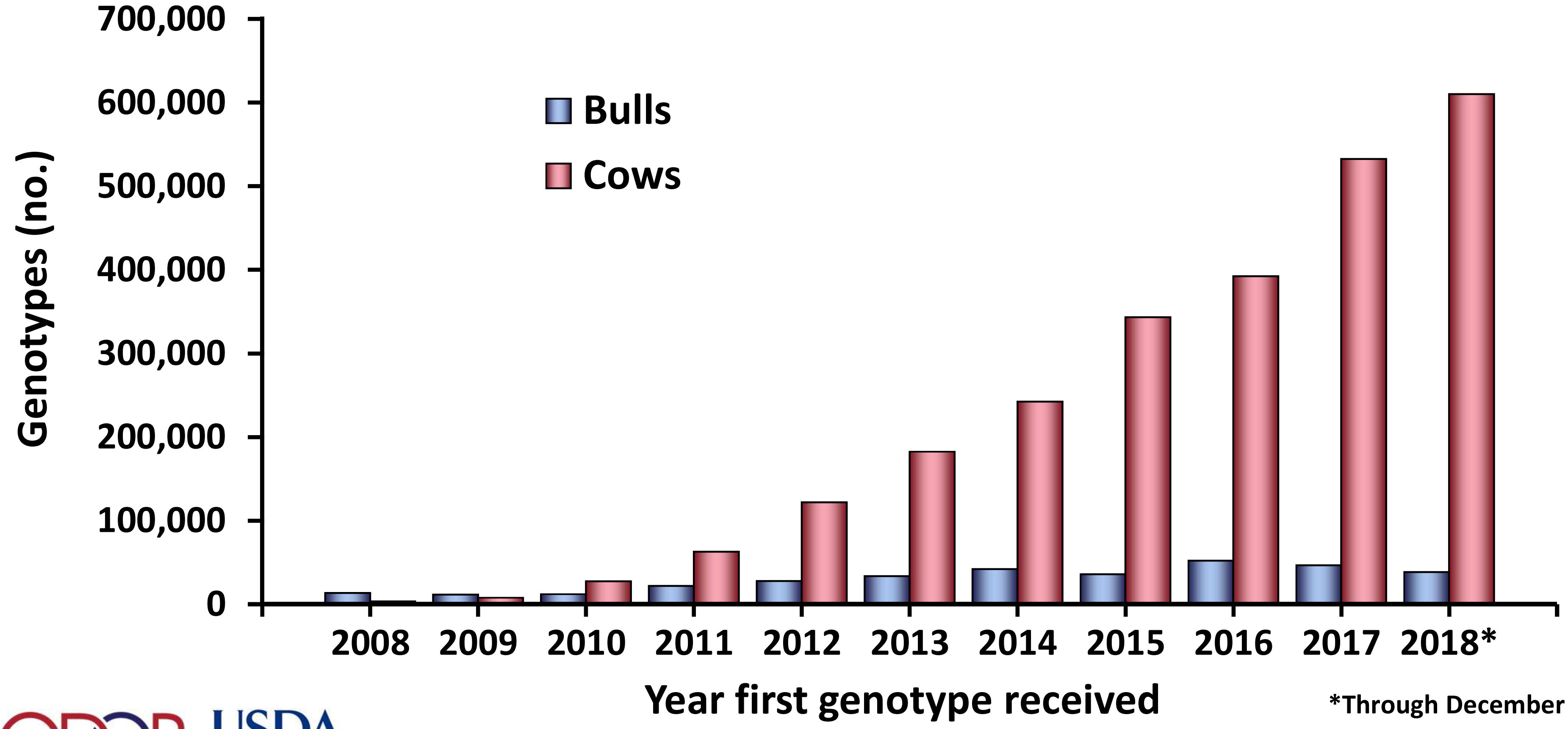
Usable genotype counts by animal sex

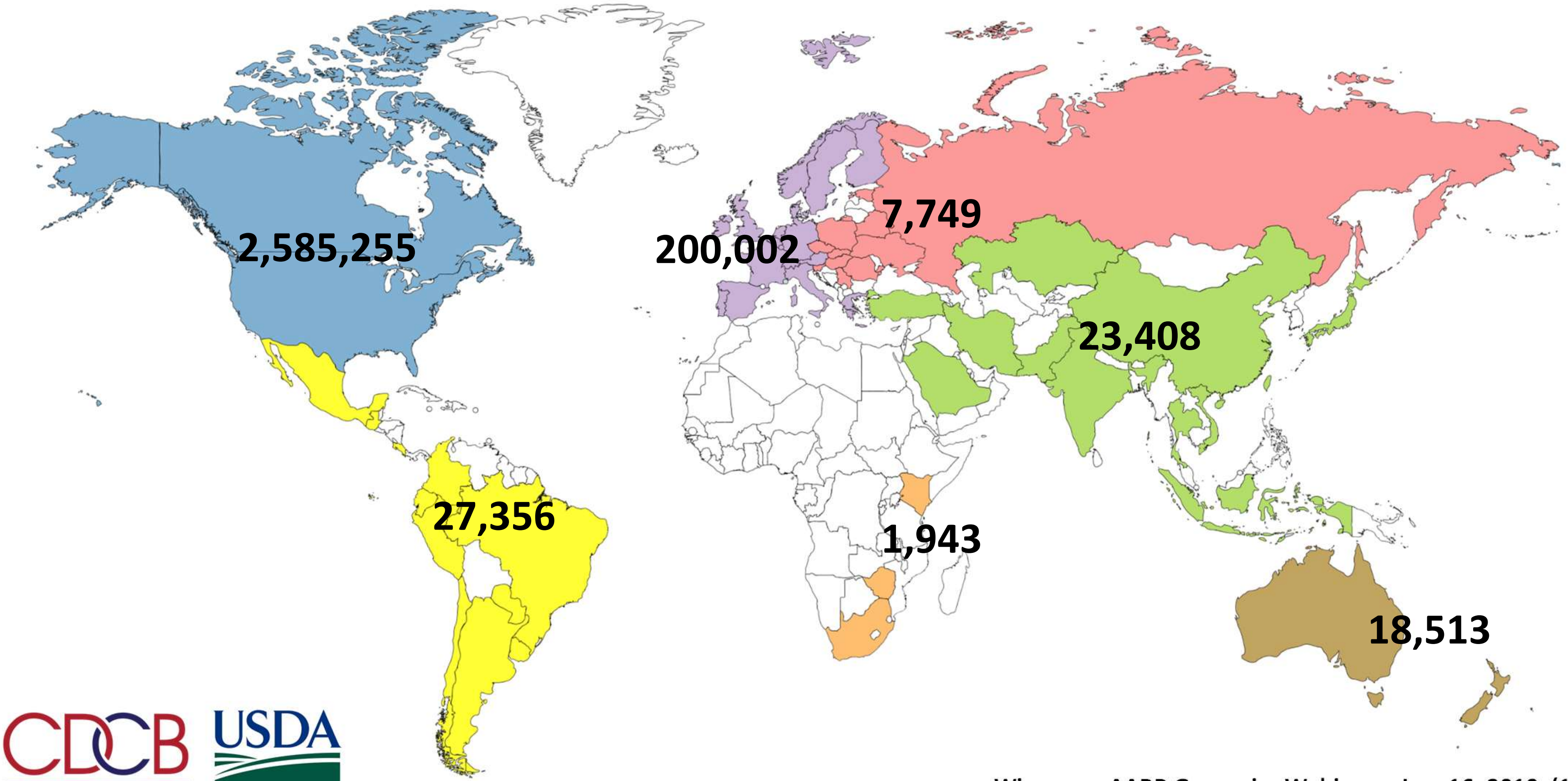


*Through December 13

International genotype exchanges

Country exchanges with U.S.	Breed	Sex	Since
Canada	All	*Both*	2009
United Kingdom, Italy	Holstein	Bulls	2011
All Europe via Interbull	Brown Swiss	Bulls	2012
Denmark	Jersey	Bulls	2014
United Kingdom (one time)	Guernsey	*Both*	2014
Japan, Switzerland, Germany	Holstein	Bulls	2016

Genotyped animals in database by region (2018)



Validation of parents

- Around 3 million animals genotyped in U.S. system
- Portion of parents validated
  - 97% of sires
  - 39% of dams
- Each genotype compared with all others to discover identical genotypes and parent-progeny relationships
- Animals with incorrect sire or dam excluded from evaluation

Parentage validation and discovery

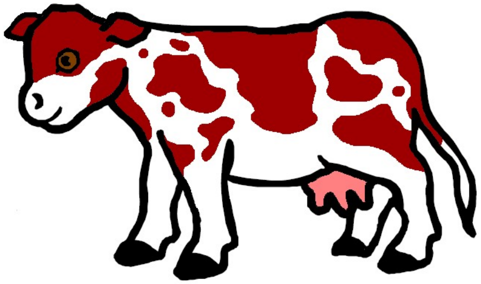
- Parent-progeny conflicts detected
  - Reported to breeds and requesters
  - Correct sire usually detected
- Maternal grandsire (MGS) checked
  - Less certain than parentage checking

Imputation

- Based on splitting genotype into individual chromosomes (maternal and paternal contributions)
- Missing SNPs assigned by observing SNPs in ancestors and descendants
- Enables use of lower cost/fewer SNP chips
- Genotypes from all chips merged by imputing SNPs not present

Gene tests (imputed and actual)

- Holstein
  - Bovine leucocyte adhesion deficiency (BLAD)
  - Complex vertebral malformation (CVM)
  - Deficiency of uridine monophosphate synthase (DUMPS)
  - Syndactyly (mulefoot)
  - Cholesterol deficiency
  - Red coat color
- Brown Swiss
  - Weaver Syndrome
  - Spinal dismyelination (SDM)
  - Spinal muscular atrophy (SMA)
- Polledness (Holstein, Jersey, Brown Swiss)



Haplotypes affecting fertility

- Rapid discovery of new recessive defects
    - Large numbers of genotyped animals
    - Affordable DNA sequencing
- Determination of haplotype location
    - Significant number of homozygous animals expected, but none observed
    - Narrow suspect region with fine mapping
    - Use sequence data to find causative mutation

Haplotypes affecting fertility

Name[1]	Chromo-some[2]	ARS-UCD location (Mbp)[3]	Current carrier frequency (%)	Earliest known genotyped ancestor
HH1	5	62.8*	2.6	Pawnee Farm Arlinda Chief
HH2	1	93.5–95.6	2.4	Willowholme Mark Anthony
HH3	8	93.8*	5.3	Glendell Arlinda Chief, Gray View Skyliner
HH4	1	2.0*	0.5	Besne Buck
HH5	9	91.8–91.9	4.8	Thornlea Texal Supreme
HH6	16	29.0–29.1	0.9	Gray View Skyliner
JH1	15	15.4*	18.4	Observer Chocolate Soldier
BH2	19	10.8*	13.3	Rancho Rustic My Design
AH1	17	63.7*	22.3	Selwood Betty's Commander
AH2	3	51.1	13.3	Oak-Ridge Flashy Kellogg

[1] BH1 and JH2 discontinued [2] *Bos taurus* (BTA) [3] Mbp = megabase pairs; * = causative mutation known

Detection of chromosomal abnormalities

- Where parent and progeny have more conflicting SNPs than allowed for a true parent-progeny relationship, location of conflicts checked

- If conflicts concentrated on a single chromosome, parent-progeny relationship accepted
  - Large deletion – animal homozygous in the region
  - Uniparental disomy – heterozygous SNPs in the region
  - 137 cases discovered so far

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Dairy Calf DNA BioBank

- Collect DNA and phenotype information from calves affected with genetic disorders, and their relatives
- Beta version of website
  - https://aipl.arsusda.gov/BioBank/
- If patterns are observed (e.g., many problems in one family), DNA is available for sequencing to identify causal change in genome and develop a diagnostic test
- To make a report, contact john.cole@ars.usda.gov

Validation of grandsires

- If parent not genotyped or not confirmed, grandsire checked
- Grandsire declared unlikely if animal and grandsire have more opposite homozygotes than threshold % (declines as possible comparisons increase)
- Possible grandsires suggested if has low percentage of conflicts and birth date reasonable
- Animals with unlikely grandsires excluded from evaluation

Use haplotypes for MGS discovery

- Include new animals with unknown or unlikely MGS in weekly evaluation calculations (confirmed sire required)
- For genotypes not qualifying for evaluation, blank conflicting pedigree and suppress release of evaluation
- Continue use of 1 SNP at-a-time comparison for PGS

Heritability

- Proportion of trait variation that results from genetics
- Measured from 0 to 100%
- Genetic improvement related to heritability
  - Selection on traits with high heritability
    → Faster genetic progress
  - Selection on traits with low heritability
    → Slower or minimal genetic progress

Heritabilities used in U.S. genetic evaluation

Trait	Heritability
Yield (milk, fat, protein)	15–29%
Conformation (type, ~17 traits)	8–51%
Longevity (productive life, cow livability)	1.3–8%
Somatic cell score (mastitis resistance)	12%
Daughter pregnancy rate	1.4%
Heifer conception rate	1%
Cow conception rate	1.6%
Service sire (direct) calving ease	8.6%
Daughter (maternal) calving ease	4.8%
Service sire (direct) stillbirth rate	0.8%
Daughter (maternal) stillbirth rate	2.1%
Gestation length (heifers, cows)	44–48%
Age at first calving (early maturity)	2.7%
Health (hypocalcemia, displaced abomasum, ketosis, mastitis, metritis, retained placenta)	0.6–3.1%

Dairy cattle traits evaluated by USDA & CDCB

Year	Trait
1926	Milk & fat yields
1977	Protein yield (& solids-not-fat)
1978	Conformation (type)
1994	Productive life, somatic cell score (mastitis resistance)
2000	Calving ease (Iowa State University, 1978–99)
2003	Daughter pregnancy rate
2006	Stillbirth rate, bull conception rate (ERCR, DRMS, Raleigh, NC, 1986–2005), milking speed
2009	Cow and heifer conception rates, genomic evaluation
2012	Mobility, calving-to-insemination interval
2016	Gestation length
2017	Cow livability
2018	Health traits (milk fever, displaced abomasum, ketosis, mastitis, metritis, retained placenta)

Evaluation of new traits

- **Age at 1st calving – To be added in 2019**
    - To be reported as Early Calving
    - Higher values mean earlier calving
- **Feed efficiency – Under development**

Recent and planned changes

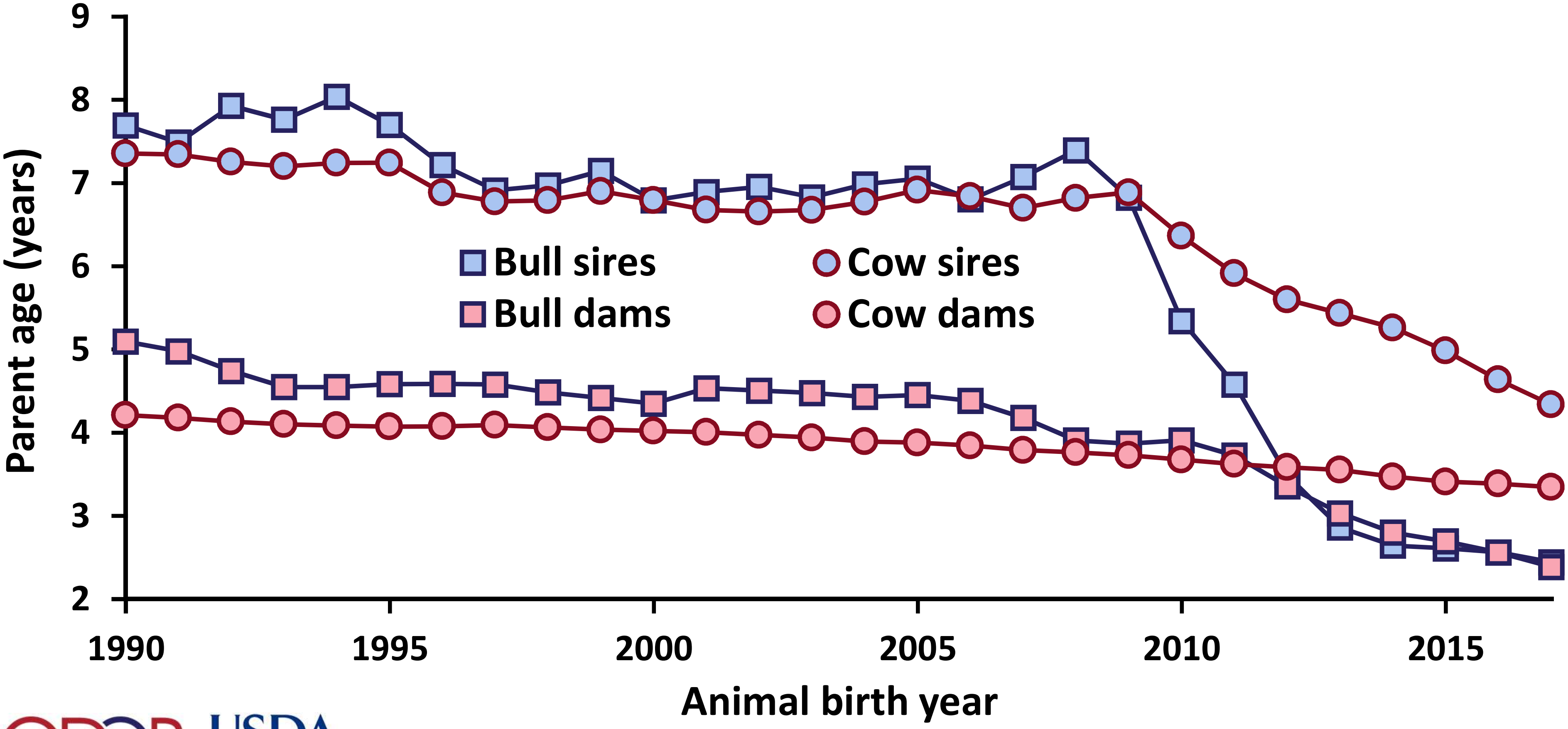
- Increase from 60,000 to 80,000 SNPs used in evaluation – December 2018
- Evaluation of crossbreds by blending purebred SNP effects – planned for April 2019

Changes Ahead by Nick Youngson CC BY-SA 3.0 Alpha Stock Images

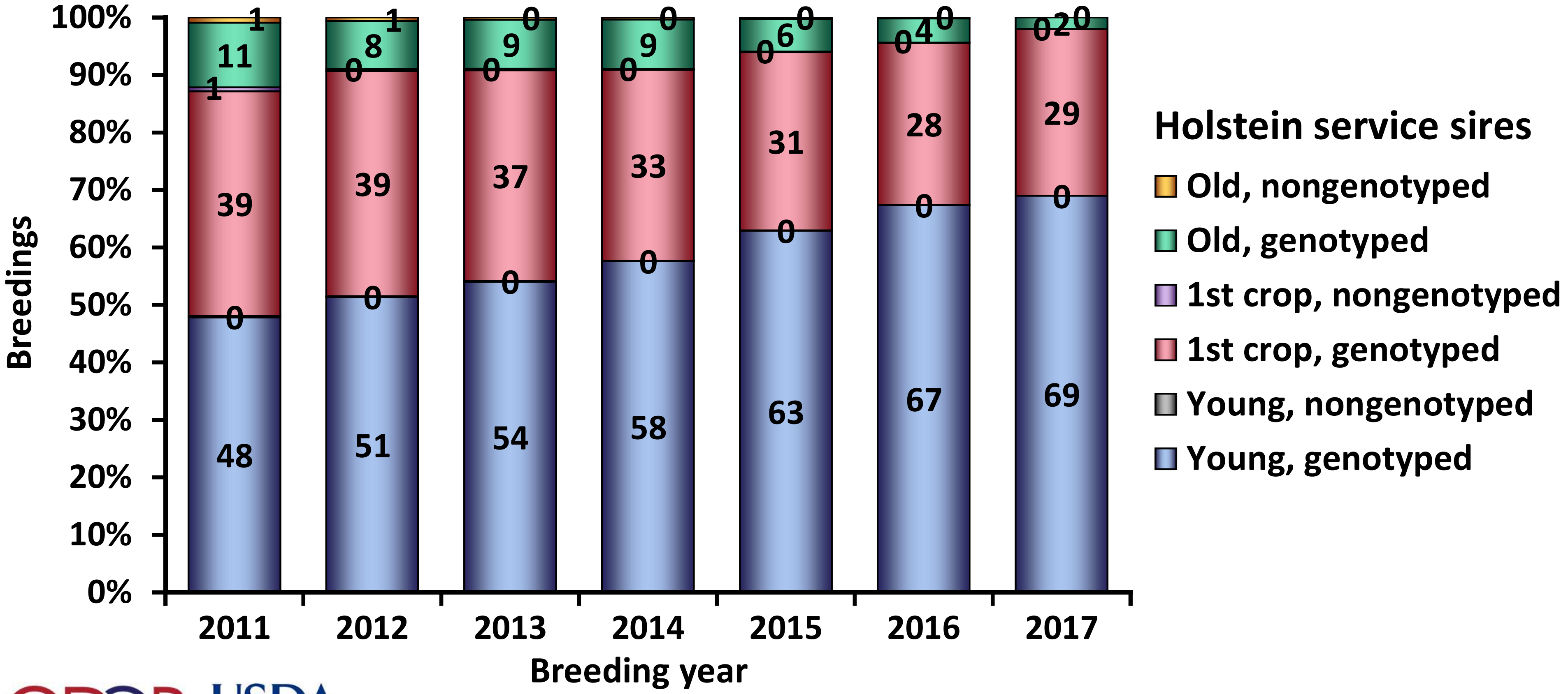
Release of evaluations

- Download from CDCB FTP site with separate files for each nominator
- Weekly release of evaluations of new animals
- Monthly release for females and bulls not marketed
- All genomic evaluations updated 3 times each year with traditional evaluations

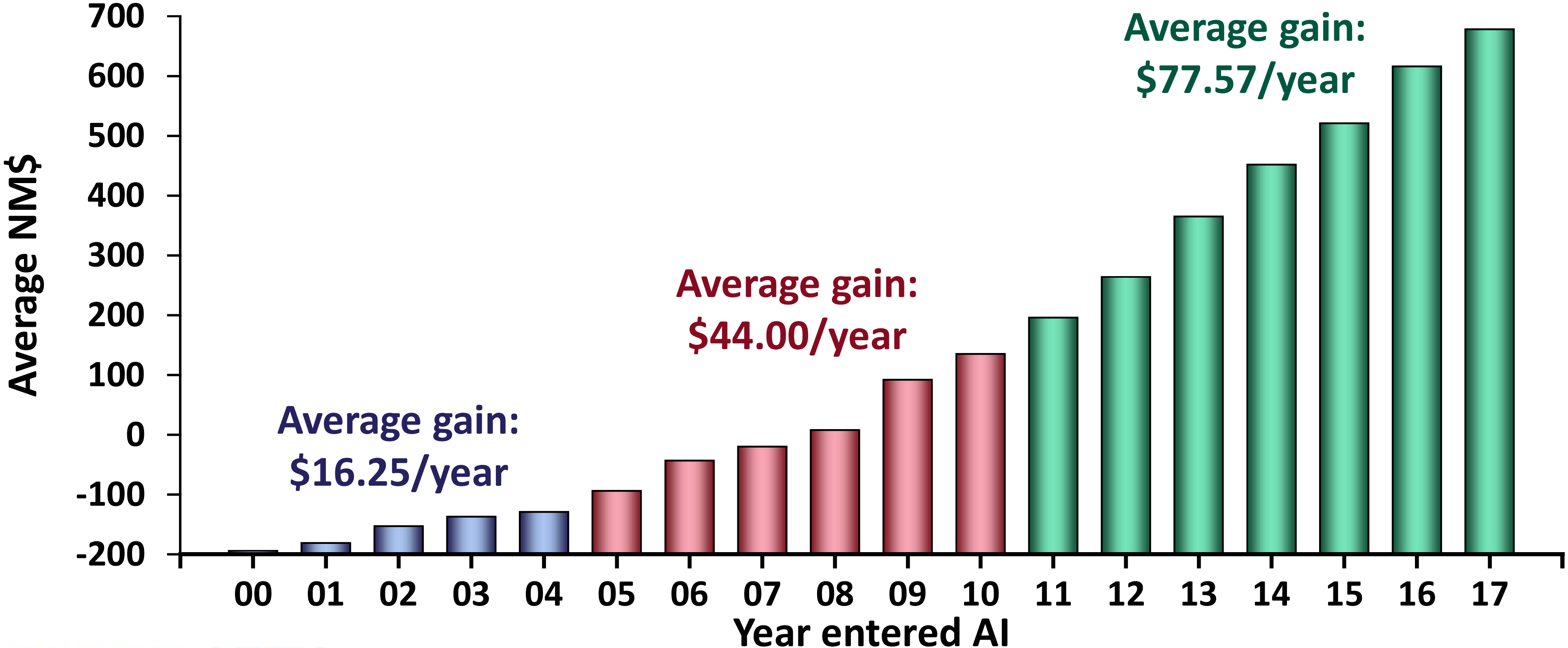
Generation interval – Holstein



AI breedings to genomic bulls



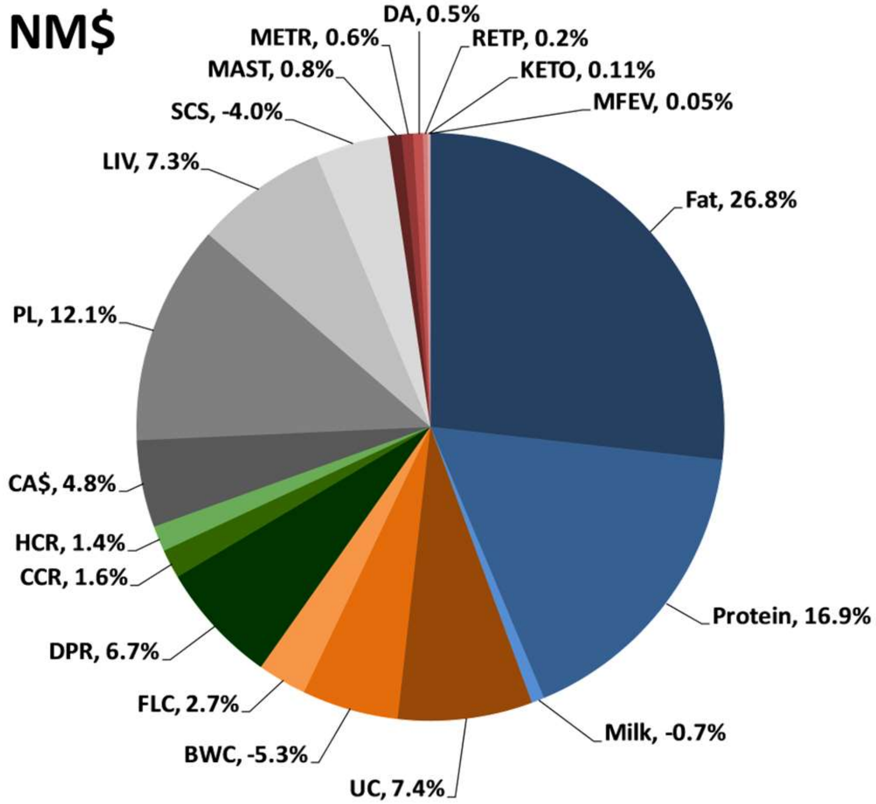
Genetic merit of marketed Holstein bulls



Genetic-economic index changes across time

	Relative emphasis on traits (%)								
Trait	PD$ 1971	MFP$ 1976	NM$ 1994	NM$ 2000	NM$ 2003	NM$ 2006	NM$ 2014	NM$ 2017	NM$ 2018
Milk	52	27	6	5	0	0	–1	–1	–1
Fat	48	46	25	21	22	23	22	24	27
Protein	…	27	43	36	33	23	20	18	17
PL	…	…	20	14	11	17	19	13	12
SCS	…	…	–6	–9	–9	–9	–7	–7	–4
BWC	…	…	…	–4	–3	–4	–5	–6	–5
UC	…	…	…	7	7	6	8	7	7
FLC	…	…	…	4	4	3	3	3	3
DPR	…	…	…	…	7	9	7	7	7
CA$	…	…	…	…	…	6	5	5	5
HCR	…	…	…	…	…	…	1	1	1
CCR	…	…	…	…	…	…	2	2	2
LIV	…	…	…	…	…	…	…	7	7
Health$	…	…	…	…	…	…	…	…	2

Relative weighting in 2018 net merit (NM$)



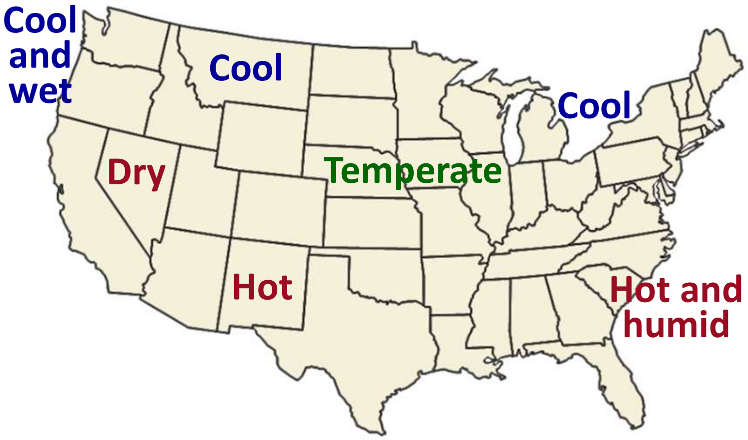
UC	Udder composite
BWC	Body weight composite
FLC	Feet-legs composite
DPR	Daughter pregnancy rate
CCR	Cow conception rate
HCR	Heifer conception rate
CA$	Calving ability (calving ease & stillbirth rate)
PL	Productive life
LIV	Livability
SCS	Somatic cell score
MAST	Mastitis
METR	Metritis
DA	Displaced abomasum
RETP	Retained placenta
KETO	Ketosis
MFEV	Milk fever

What we expect in the future

- Increasing number of cows genotyped
- Falling cost per SNP genotyped
- Increased accuracy of genomic evaluations from more informative SNPs
- Genomic evaluations on more traits to predict economic merit more accurately
- Increased use of genomics in mating programs

Why is the U.S. a leader?

- Population size
- Selection intensity
- Focus on dairy breeds
- Diverse environments
- Competitive AI industry
- Independent evaluations



Benefits of genomics

- Determine genetic merit of animals at a young age
- Increase selection intensity
- Increase accuracy of selection
- Reduce generation interval
- Increase rate of genetic gain
- Identify genetic defects and reduce their frequency
- Parentage discovery
- Herd management
  - Cull low-end replacement animals earlier
  - Breed lower merit animals to beef bulls

Summary

- U.S. genetics recognized and used around the world as “the source” in many breeding programs
- Largest genetic base and high selection intensity produces elite bulls and cows
- Genomics revolutionized animal breeding and brought excitement to dairy genetics
- International collaboration important to program success

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Questions?