

Genomic selection in the USA

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Highlights of U.S. system

- Nearly 700,000 animals genotyped in 2018
- 67% of AI breedings to genomic bulls
- Genomic relationship between genotyped cows and marketed bulls provided to avoid matings that result in high inbreeding
- Evaluations of all animals updated monthly
- Evaluations on new animals released weekly



Government–industry collaboration

- Animal Genomics and Improvement Laboratory **(AGIL)**, Agricultural Research Service, U.S. Department of Agriculture **(USDA)**
 - Responsible for research and development to improve the evaluation system
 - **Located in Beltsville, Maryland**
- Council on Dairy Cattle Breeding **(CDCB)**
 - Responsible for approving changes, receiving data, and computing and delivering U.S. genetic evaluations for dairy cattle
 - **Located in Bowie, Maryland**

Funding

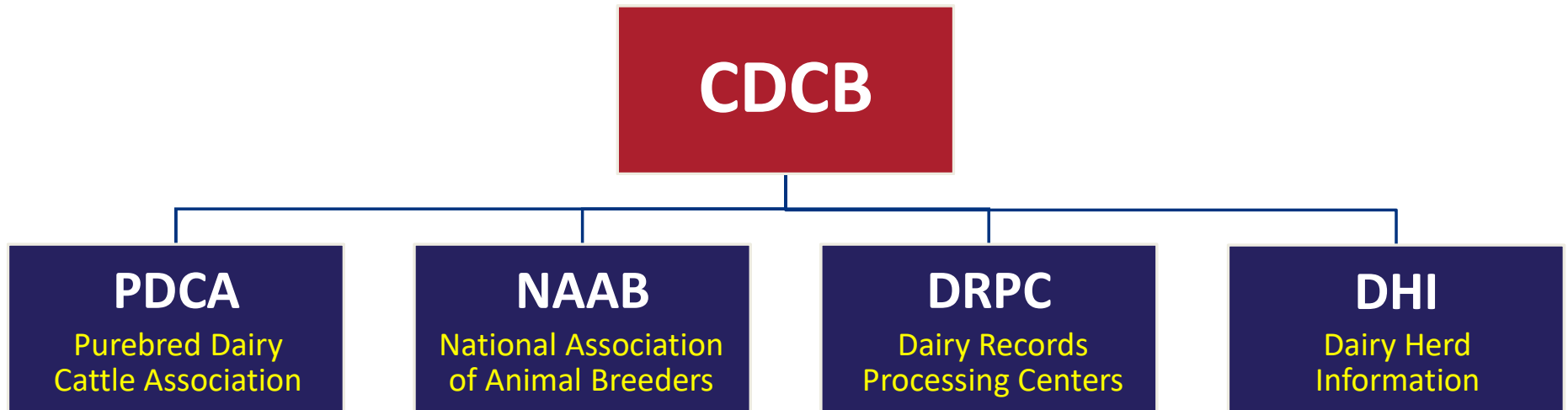
- CDCB evaluation calculation and dissemination funded by fee system
 - Based on animals genotyped
 - ~66% of revenue from bulls
 - Credits for herds that contribute more information
- USDA research on evaluation methodology funded by U.S. Federal Government



U.S. dairy genomics history

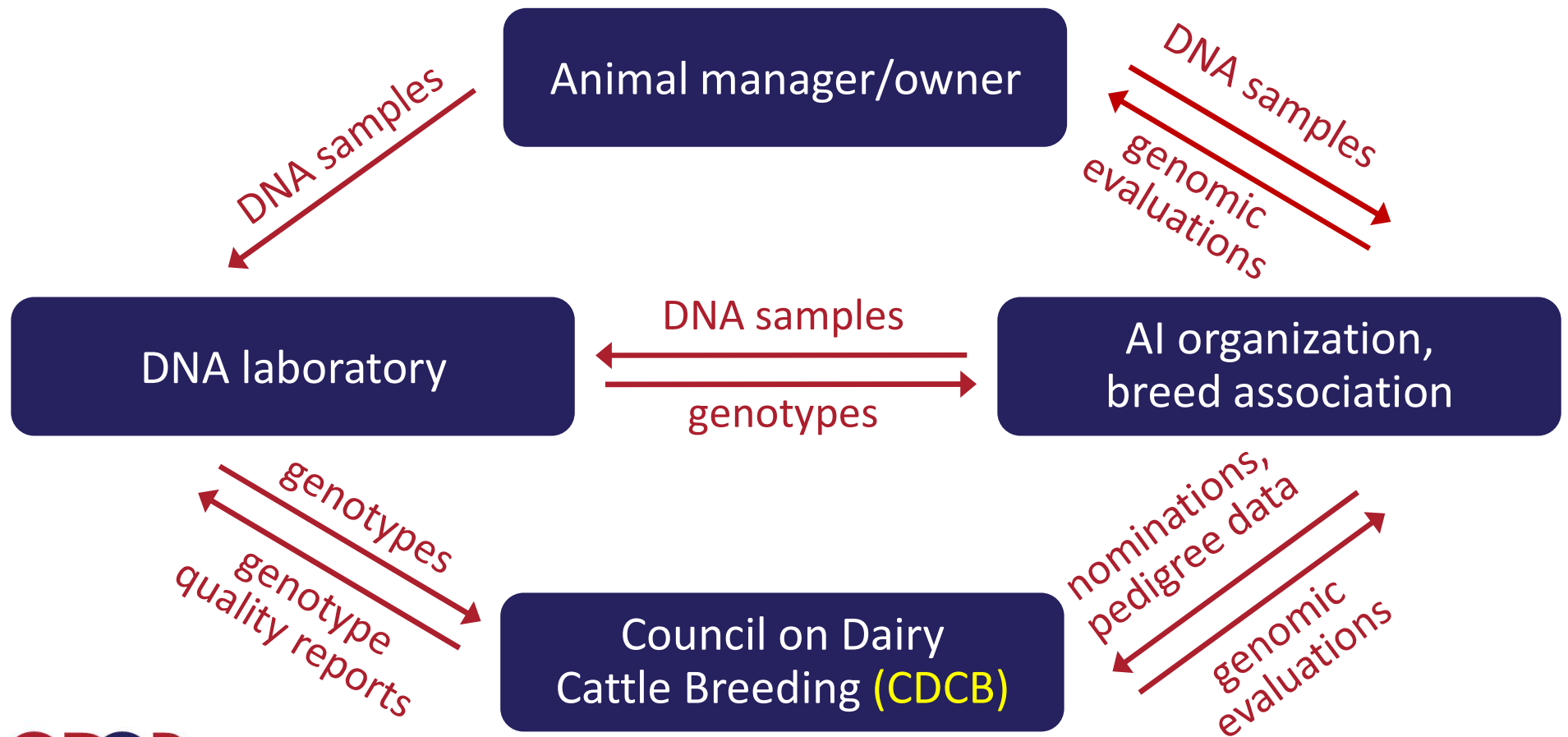
- Dairy DNA repository (Canada, U.S.) 1992
- Cattle genome sequenced 2004
- Illumina 50K SNP BeadChip 2007
- Official genomic evaluations (Holstein, Jersey, Brown Swiss) 2009
- High-reliability, low-density chip 2011
- Genomic evaluations transferred from USDA to CDCB 2013

Council on Dairy Cattle Breeding (CDCB)



- 3 members from each organization
- Total of 12 voting members
- 2 nonvoting industry members

Genomic data flow



DNA source – samples sent to genotyping labs (2018)

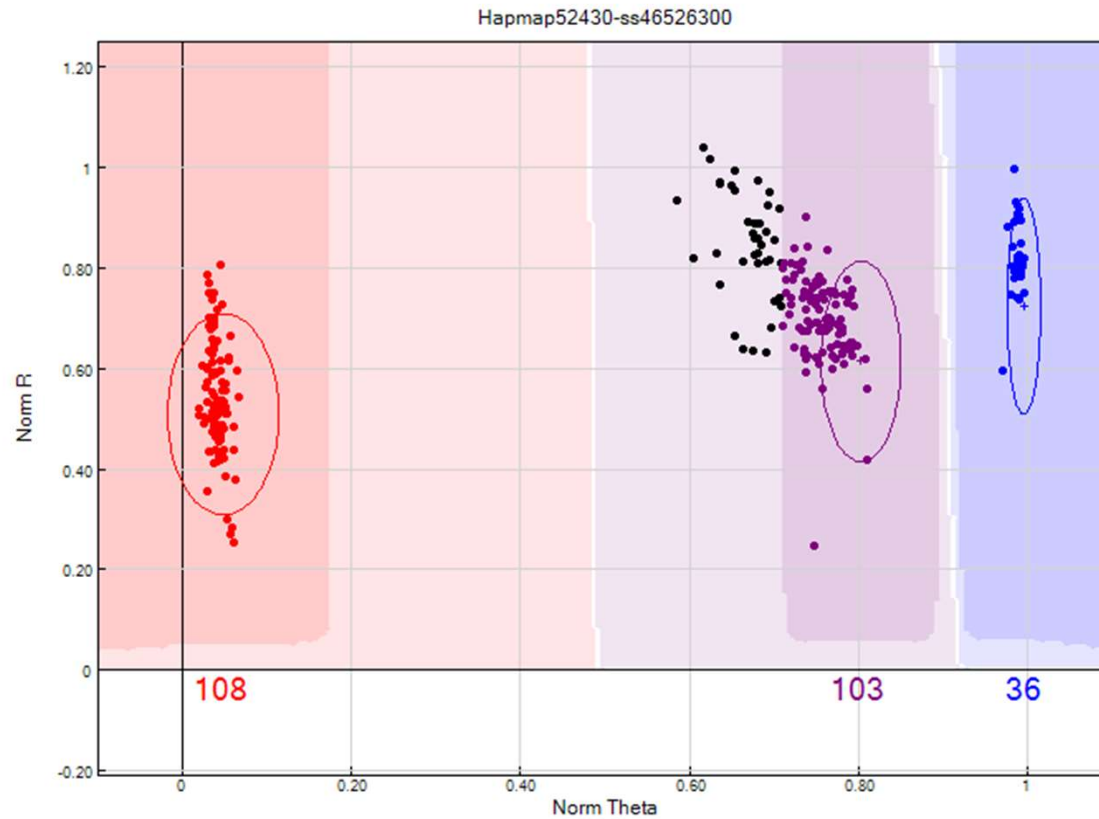
Source	Samples (no.)	Samples (%)
Blood	14,656	2
Hair	102,229	14
Nasal swab	656	<1
Semen	319	<1
Tissue	579,255	81
Unknown	17,048	2

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

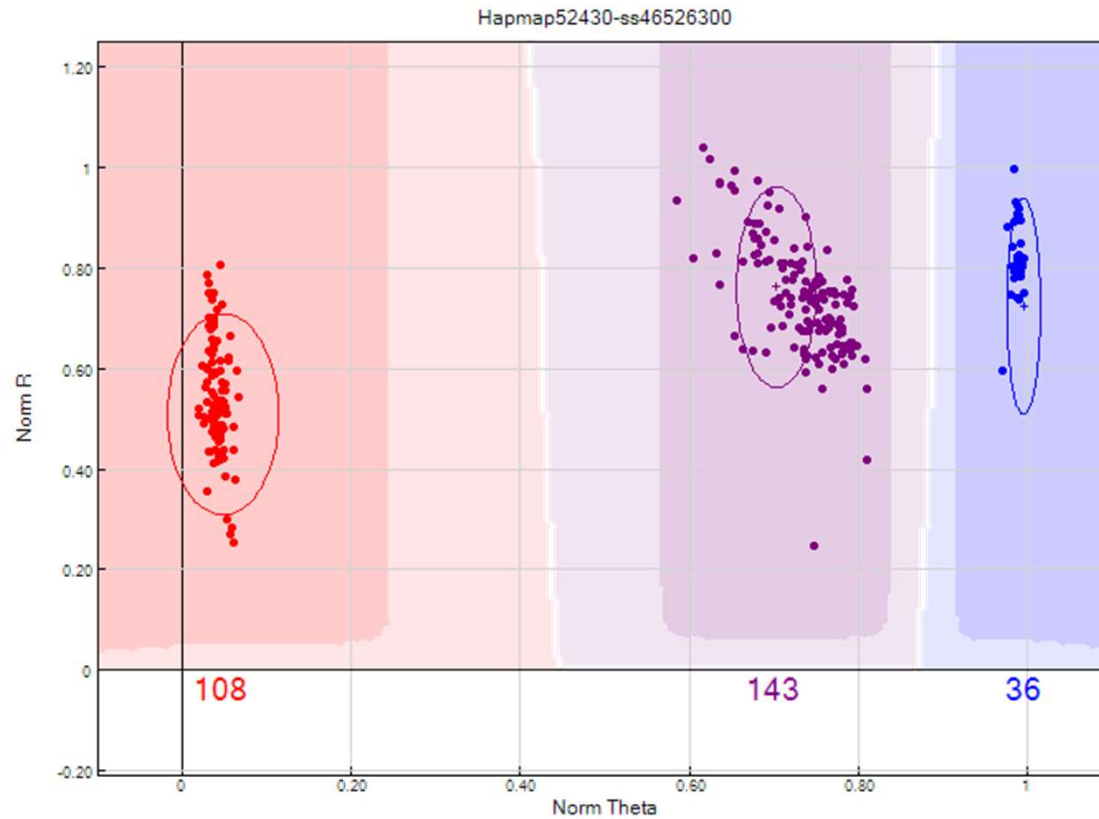


Before clustering adjustment



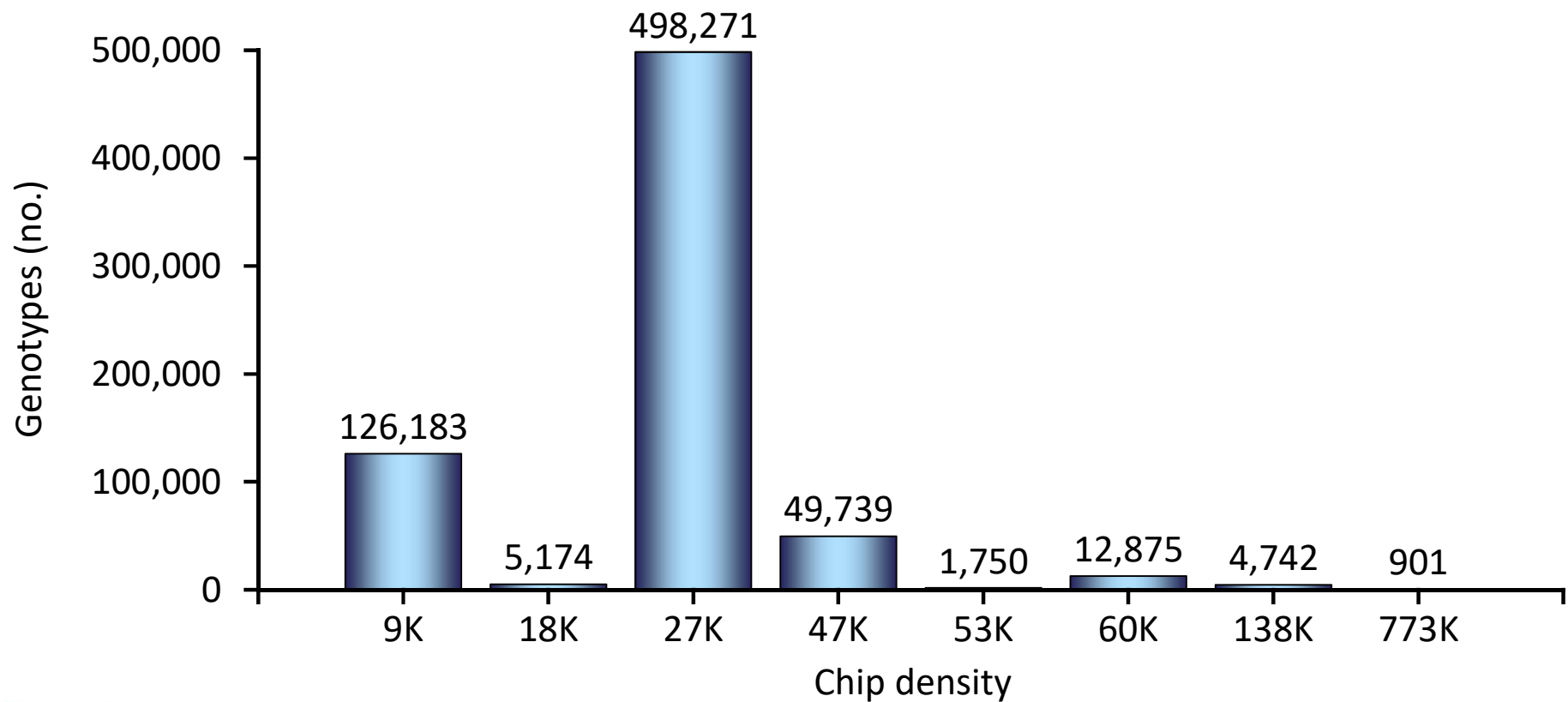
86%
call
rate

After clustering adjustment

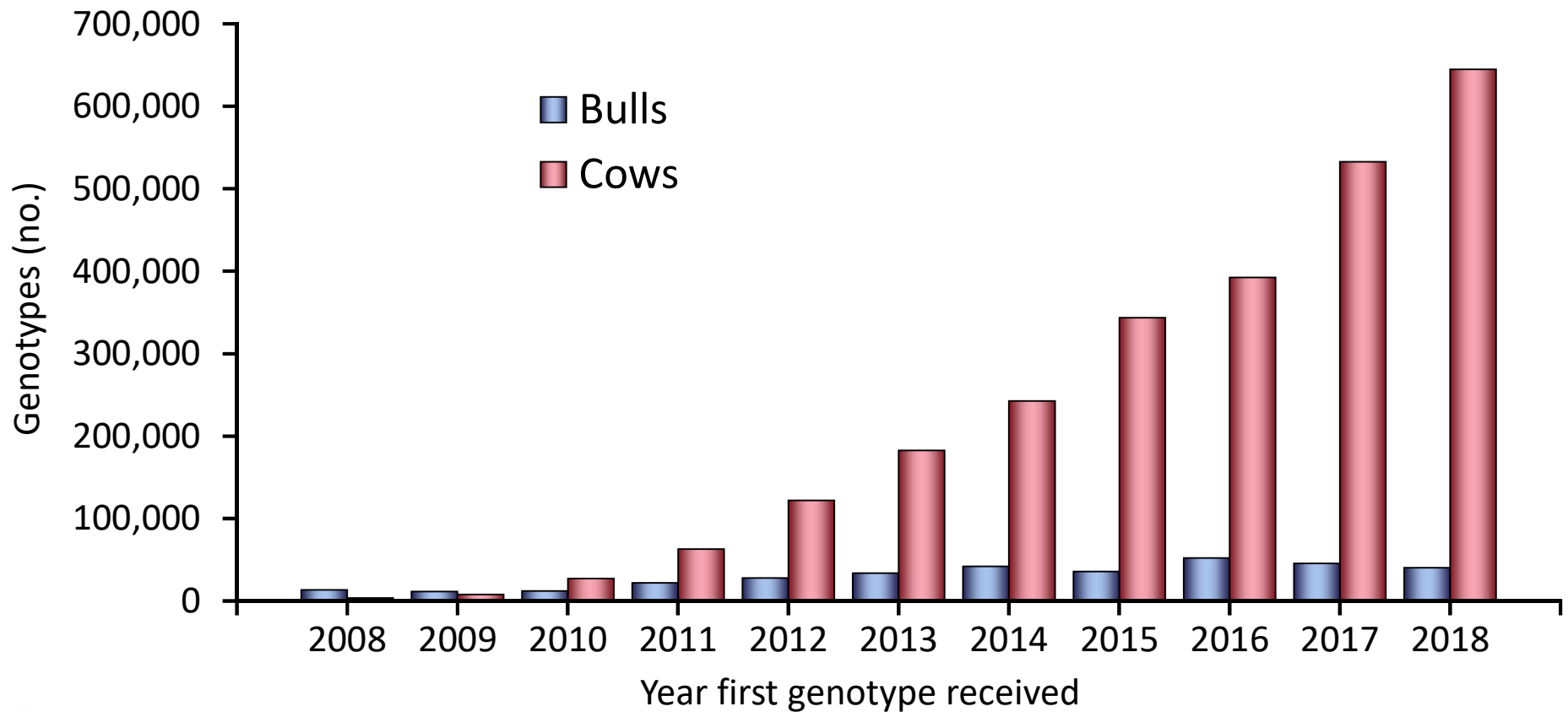


100%
call
rate

Genotype counts by chip density (2018)



Usable genotype counts by animal sex

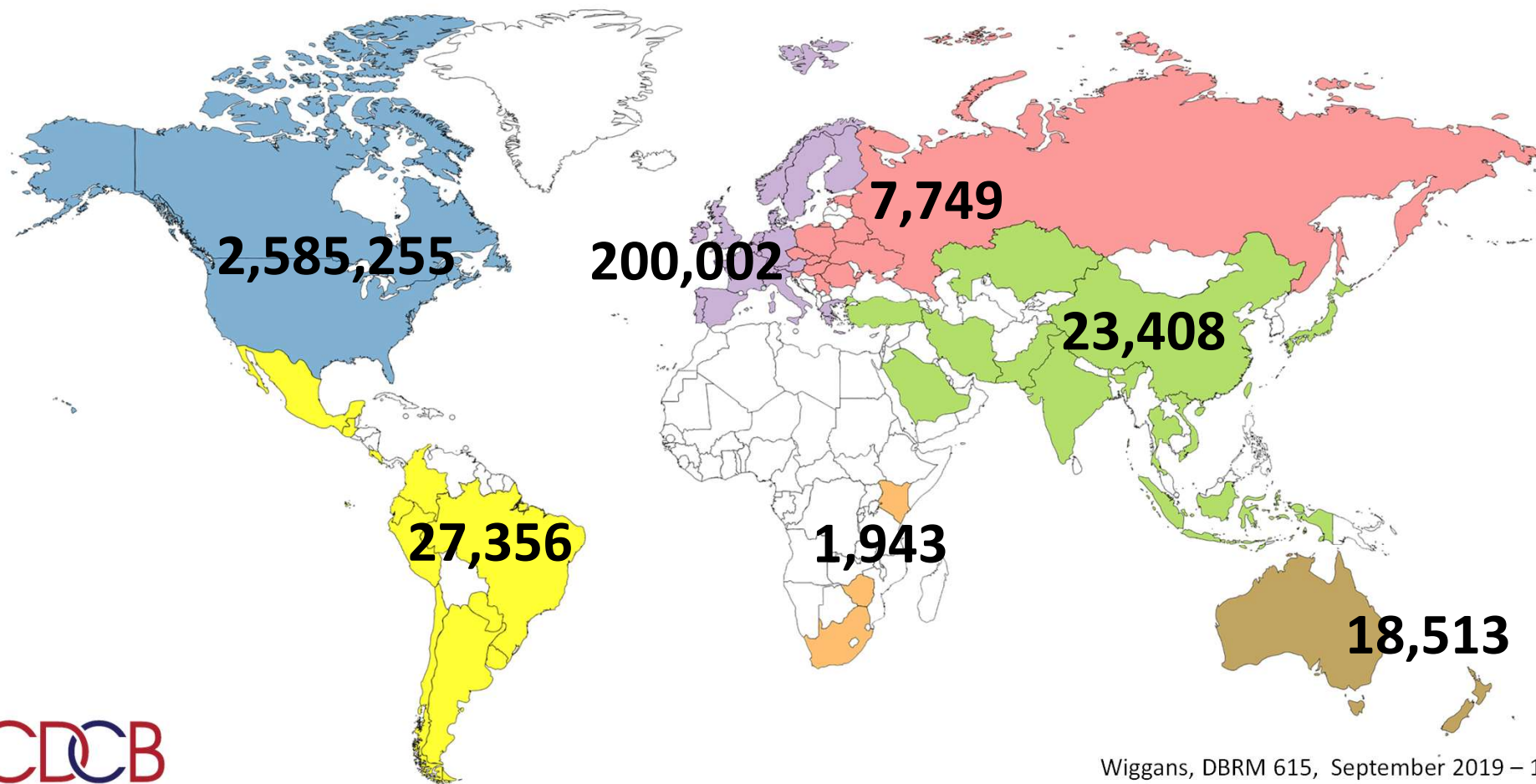


International genotype exchanges

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 (1 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

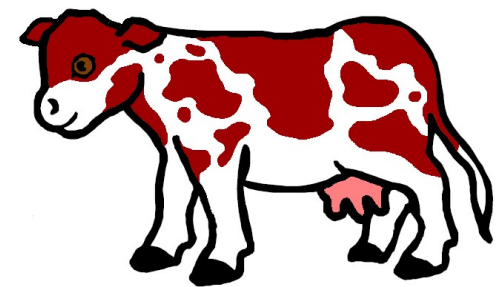


Imputation

- 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	Chromosome 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

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

Detection of chromosomal abnormalities

- Location of conflicts checked if parent and progeny have more conflicting SNPs than allowed for true parent-progeny relationship
- Parent-progeny relationship accepted if conflicts concentrated on single chromosome
 - Large deletion – animal homozygous in the region
 - Uniparental disomy – heterozygous SNPs in the region
 - 152 cases discovered so far

Validation of grandsires

- Grandsire checked if parent not genotyped or not confirmed
- Grandsire declared unlikely if animal and grandsire have more opposite homozygotes than threshold percentage (declines as possible comparisons increase)
- Possible grandsires suggested if 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**)
- Blank conflicting pedigree and suppress release of evaluation for genotypes not qualifying for evaluation
- Only 1 SNP-at-a-time detection of opposite homozygotes available for paternal grandsire

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 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

- Early first calving – April 2019
 - Calculated from age at first calving
 - Higher values mean earlier calving
- Feed efficiency – Under development



Application to more traits

- Animal's genotype good for all traits
- Traditional evaluations required for accurate estimates of SNP effects
- Traditional evaluations not currently available for heat tolerance or feed efficiency
- Research populations could provide data for traits that are expensive to measure
- Will resulting evaluations work in target population?

Recent changes

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



Changes Ahead by [Nick Youngson](#) CC BY-SA 3.0 Alpha Stock Images

Evaluation of crossbreds

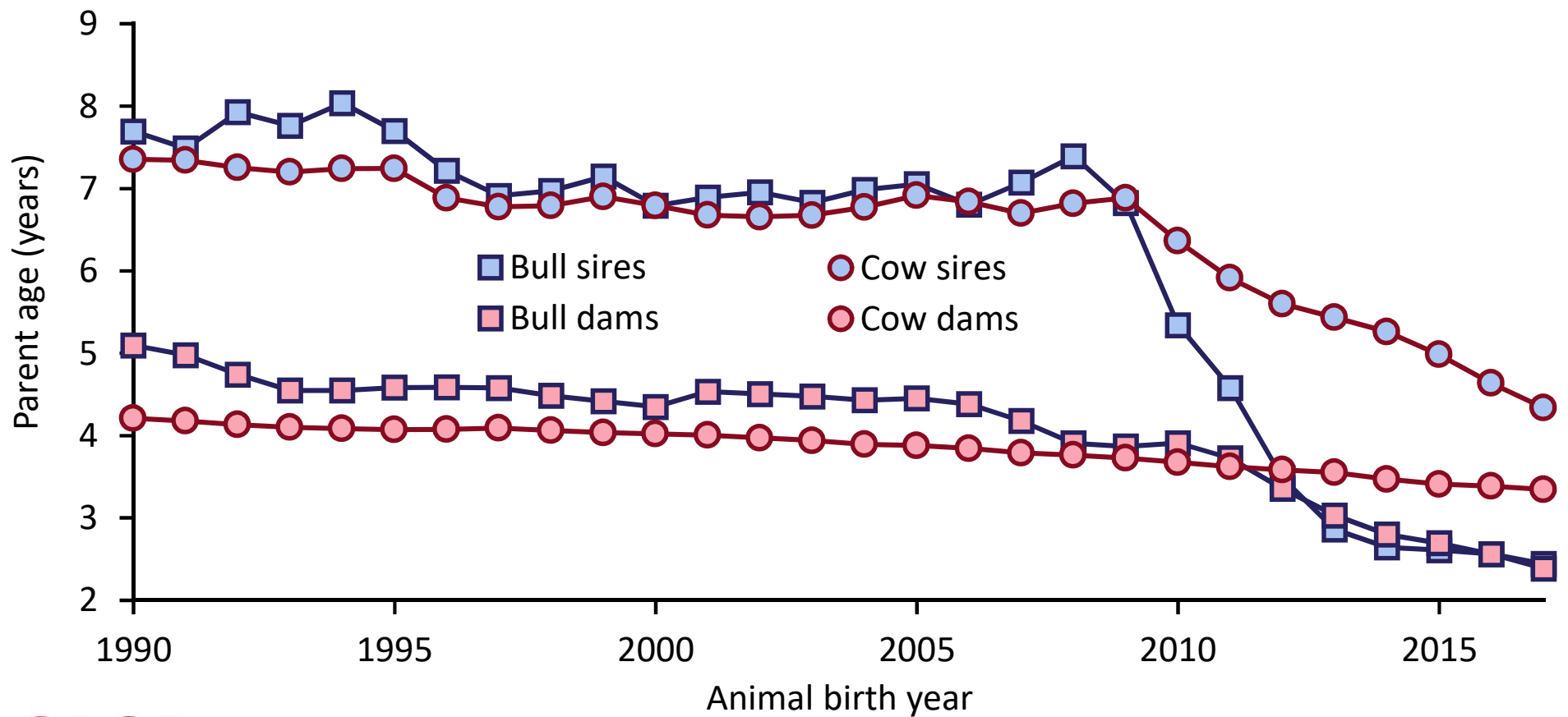
- Breed proportions called breed base representation (BBR) estimated as 5 genomic traits (Ayrshire, Brown Swiss, Guernsey, Holstein, Jersey) from purebred animals
- Animals with highest BBR < 90 evaluated by applying SNP effect solutions from each breed and then weighting by BBR
- Reference population limited to BBR ≥ 94
- Type, calving, and health traits not blended because not comparable or not available for all breeds

Release of evaluations

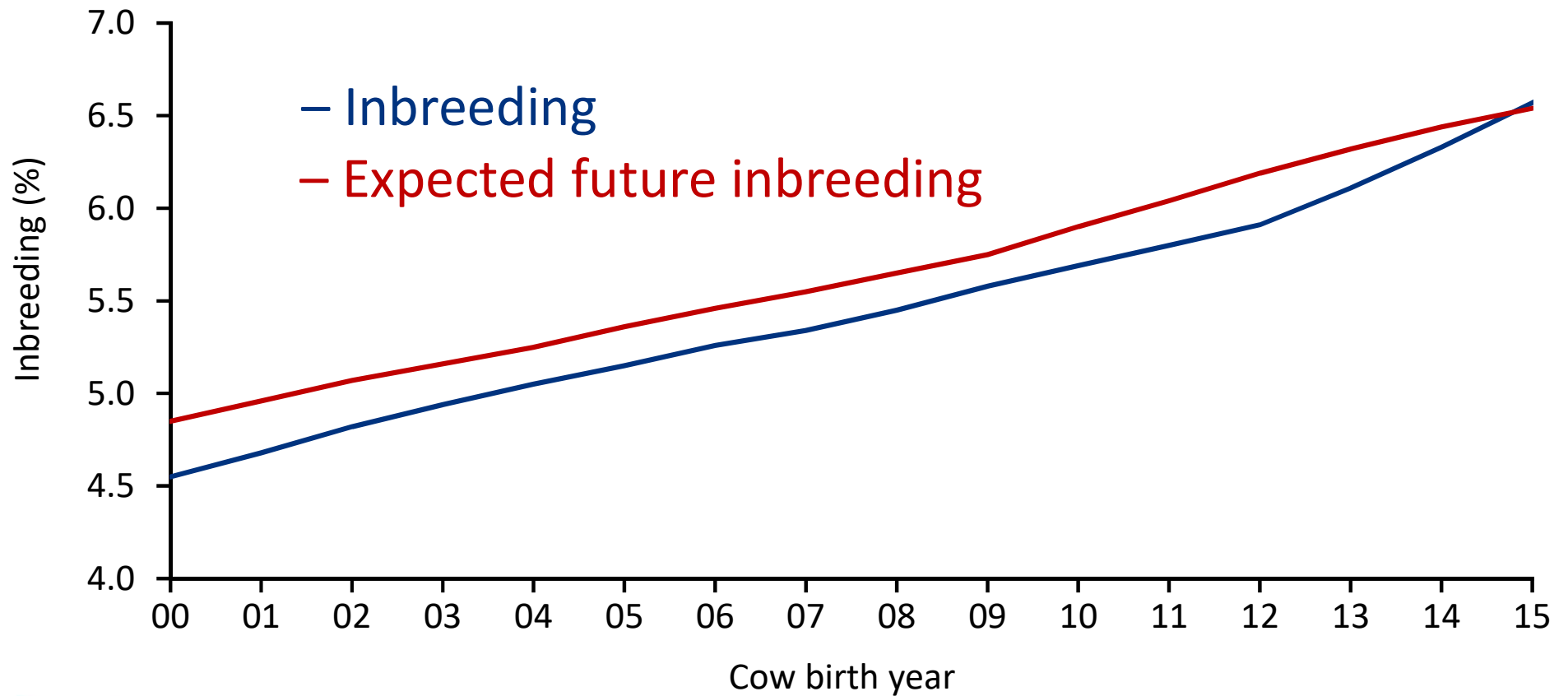
- Download from CDCB FTP site with separate files for each nominator
- Weekly release of evaluations of new animals
- Monthly release for females and bulls not marketed
- All genomic evaluations updated 3 times each year with traditional evaluations



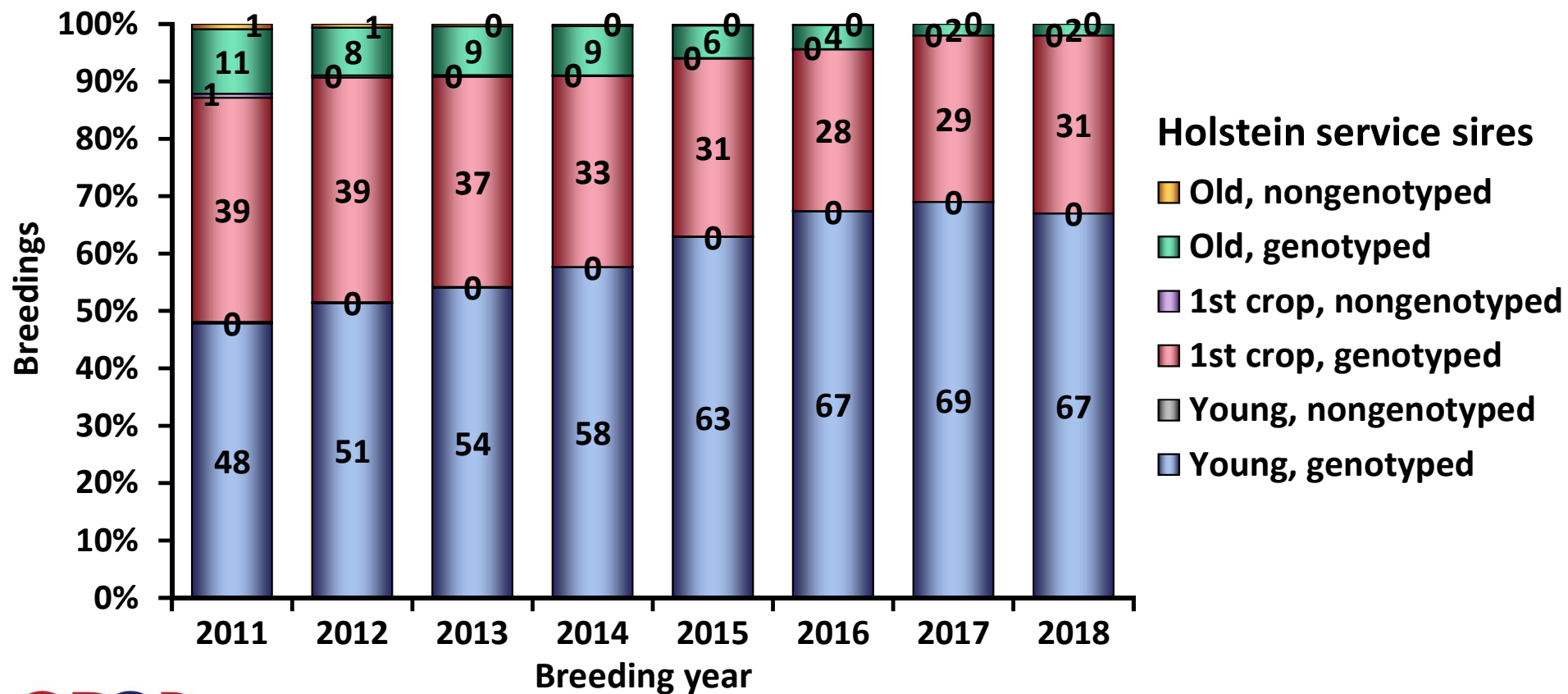
Generation interval – Holstein



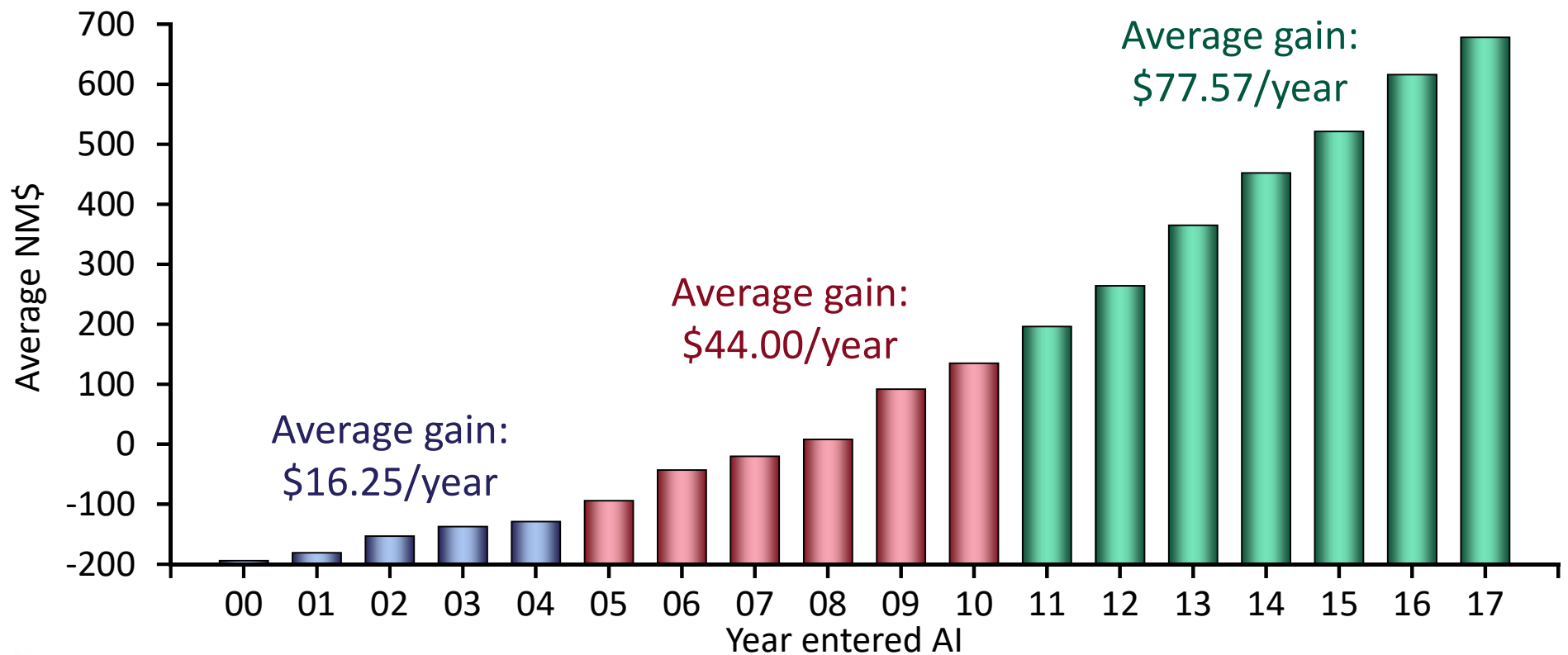
Inbreeding for Holstein cows



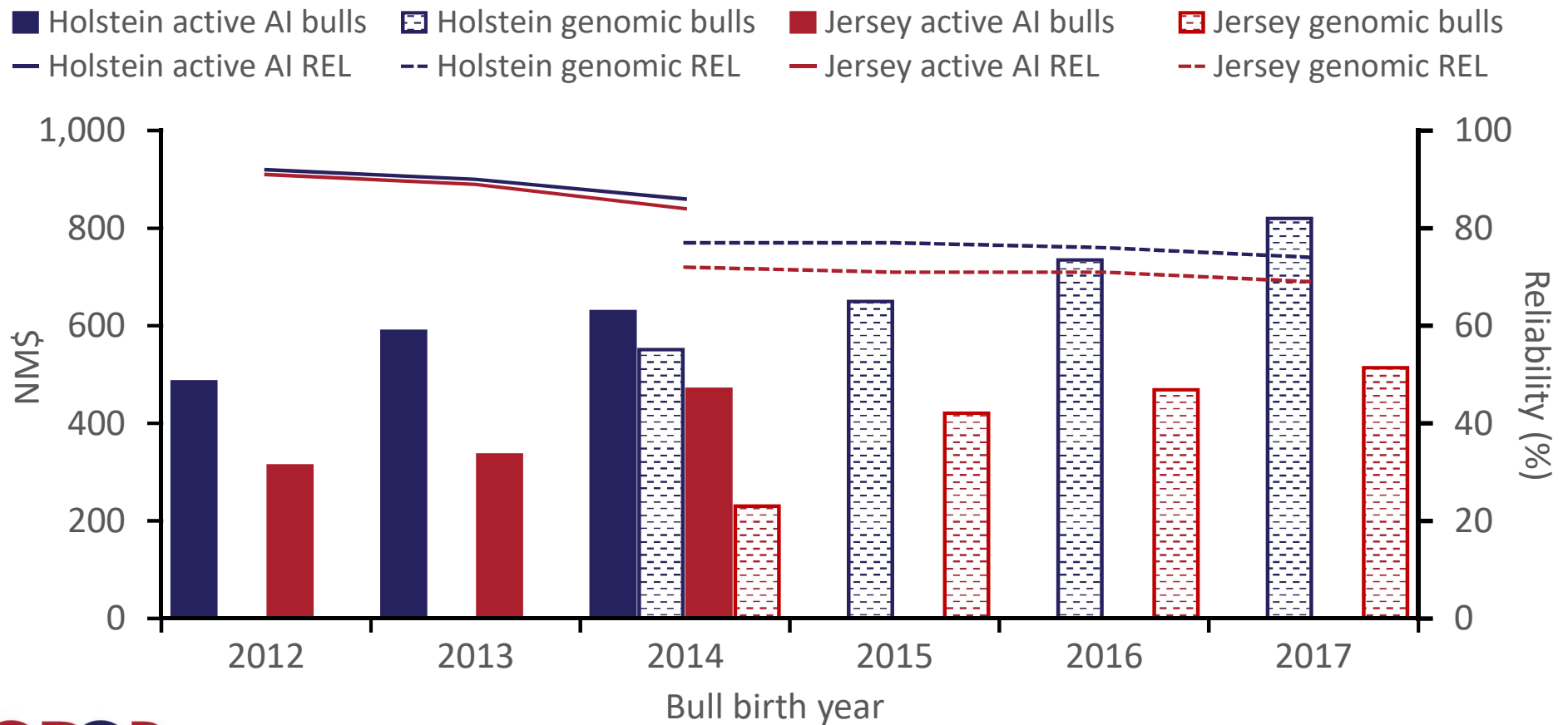
AI breedings to genomic bulls



Genetic merit of marketed Holstein bulls



Net merit of active AI and genomic bulls



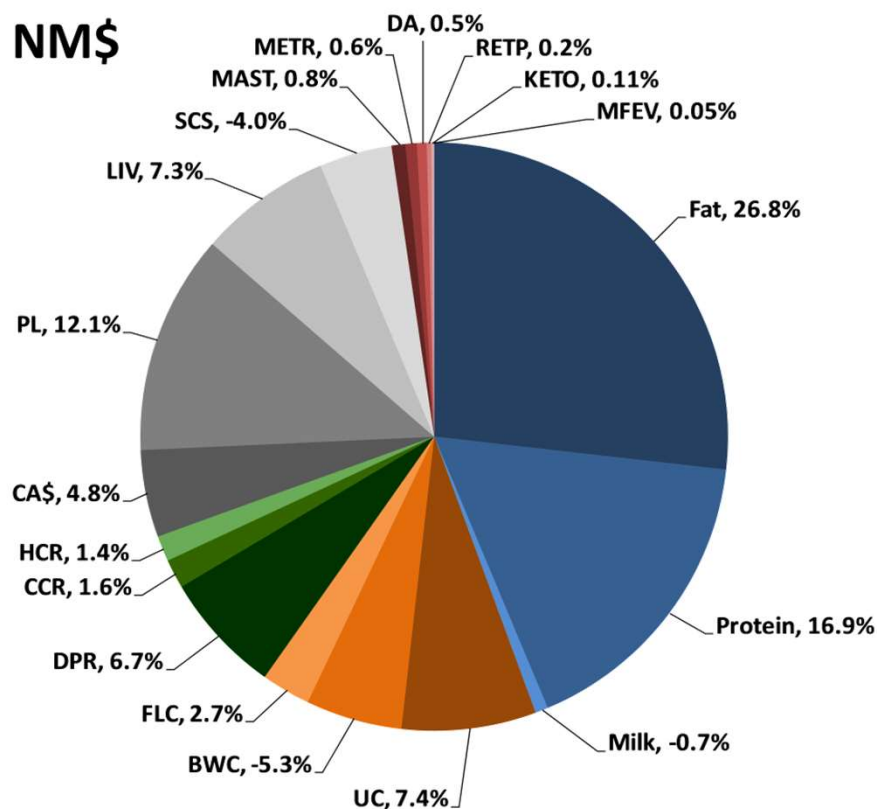
Genetic-economic index changes across time

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\$)

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 genotype females?

- Improve accuracy of culling and breeding decisions
- Breeding
 - Cows to flush
 - Cows to breed with sexed semen
 - Cows to breed to beef bulls
- Improved avoidance of inbreeding
- More accurate culling

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
- International collaboration important to program success

Acknowledgments & disclaimers

- Research support funded through USDA-ARS project 8042-31000-002-00, “Improving dairy animals by increasing accuracy of genomic prediction, evaluating new traits, and redefining selection goals”
- Mention of trade names or commercial products in this presentation is solely for the purpose of providing specific information and does not imply recommendation or endorsement by CDCB; CDCB is an equal opportunity provider and employer

