



# European Holstein – Red Holstein Conference 2009



Effects of genomic selection on breeding value estimation and international comparisons

Reinhard Reents

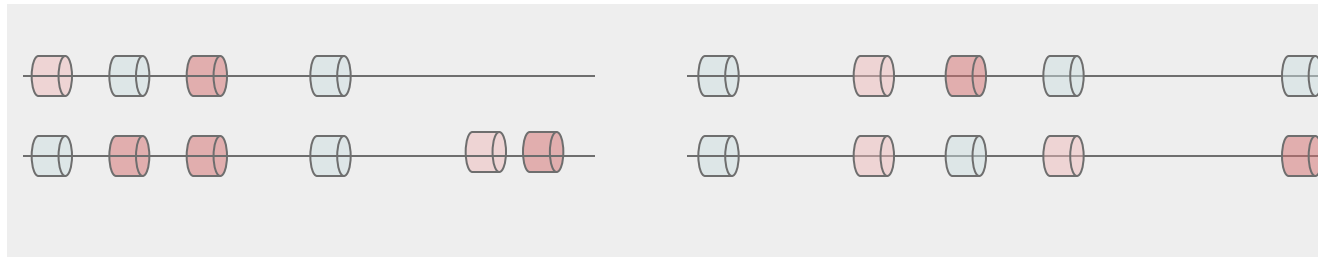
vit, IT solutions for Animal Production  
Chairman of the Steering Committee of Interbull



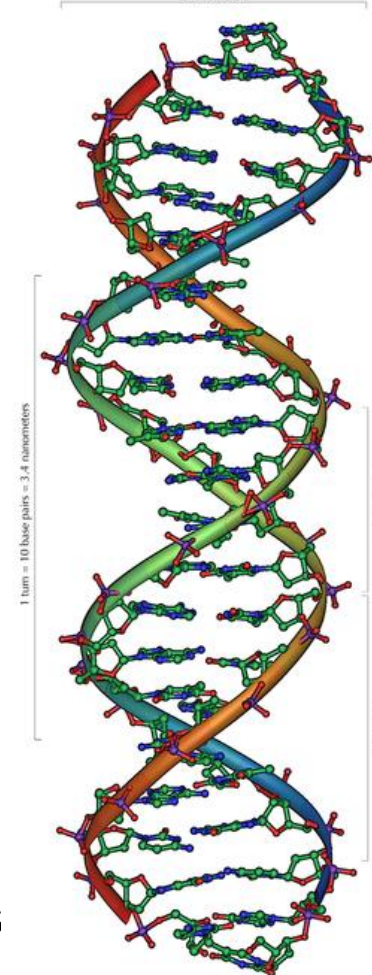


## Knowledge about genomics

- Watson und Crick 1953 Model of double helix →
  - (structure of DNA where two chains are held together by hydrogen bonds in a double spiral)
- But no information about effect of individual genes/animals:



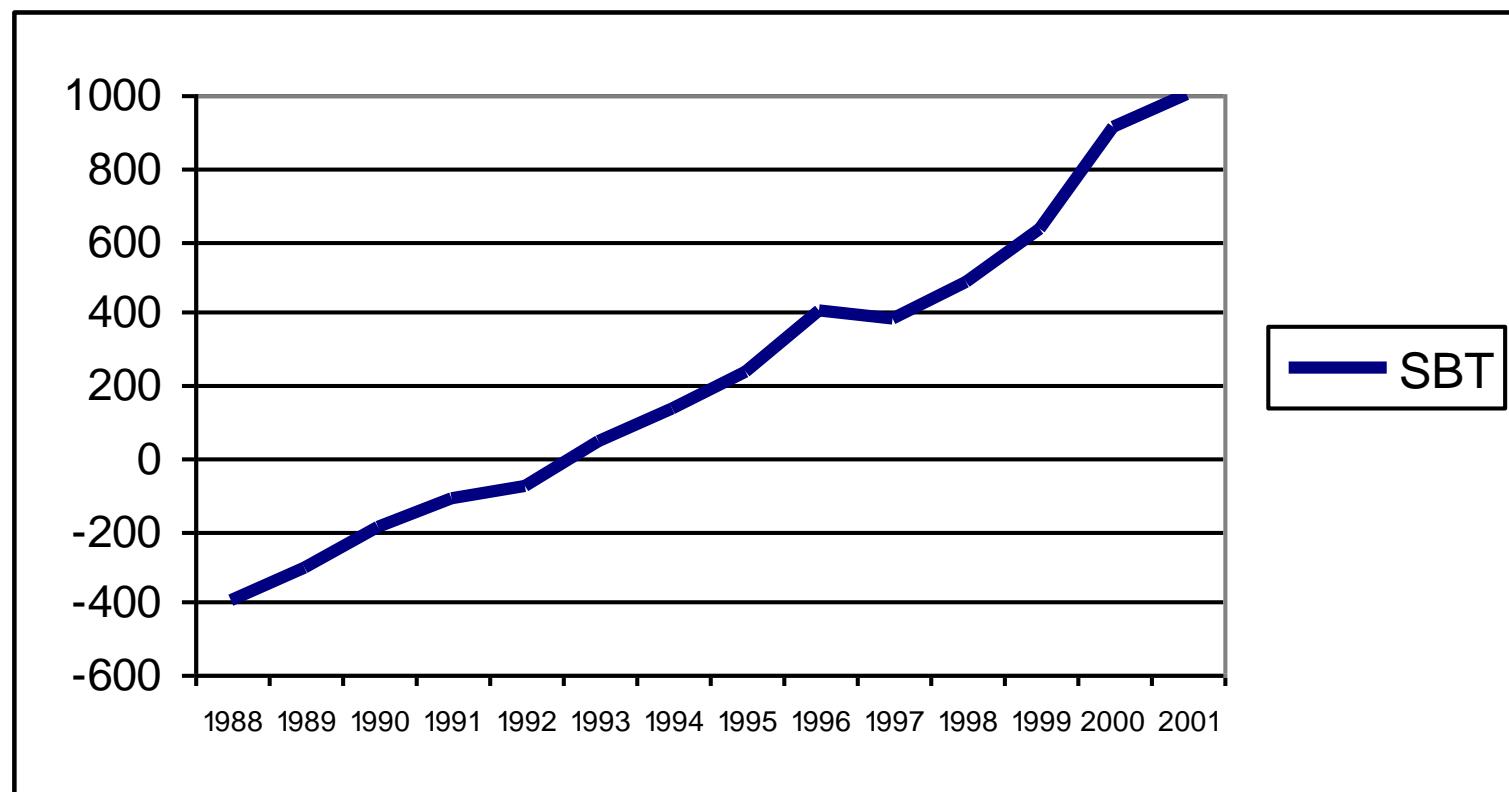
- genetic evaluation separates **phenotypic information** (eg 9850 kg milk) in **genetic component** (eg +1430 kg milk) and **environment**
- Ranking is based on estimated breeding values (EBVs)
  - Very efficient in dairy cattle





# Genetic trend in German Holstein bulls

EBV Mkg



Year of birth of AI bulls





but



## ■ Genetic gain / costs

- High generation interval due to progeny test
  - Expensive
  - Genetic gain per year not very high
- Reliability of a pedigree index ( $=0,5 \text{ EBV sire} + 0.5 \text{ EBV dam}$ ) is low (25 – 35%)
- Reliability of a cow EBV < lower as  $r^2$  of a bull EBV

## ■ Aim:

- Increase of reliability of young animals

## ■ Solution → use of genomic informationn





# SNP - genotyping



- SNP = Single-nucleotide polymorphism
- Genotype = Which alleles of the nucleotides **A-T,C-G** an animal carries
- Genome = contains 3 billion base pairs
- Ca. 50.000 SNPs at a cost of about 200 EUR

Genotype:

Tier 1:	...AGGCACC GCAATCCACG GAGGC <b>T</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	<b>TT</b>
	...AGGCACC GCAATCCACG GAGGC <b>T</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	
Tier 2:	...AGGCACC GCAATCCACG GAGGC <b>A</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	<b>AA</b>
	...AGGCACC GCAATCCACG GAGGC <b>A</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	
Tier 3:	...AGGCACC GCAATCCACG GAGGC <b>T</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	<b>AT</b>
	...AGGCACC GCAATCCACG GAGGC <b>A</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	
Tier n:	...AGGCACC GCAATCCACG GAGGC <b>A</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	<b>AA</b>
	...AGGCACC GCAATCCACG GAGGC <b>A</b> ACGC CCTCACC GGA GGTTCGCTC TCCACGG...	

Eg position on Chromosom 6 # 43.675.239

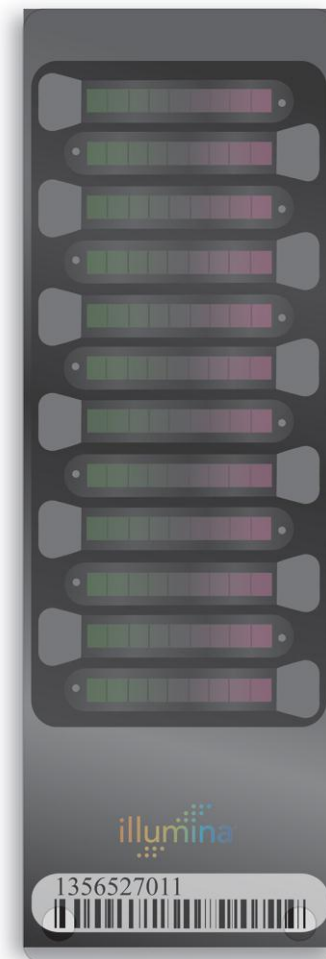




# Illumina cattle SNP-Chip: BovineSNP50 Beadchip



- Number of SNPs: 54.001
- Eg informative in Holsteins: 42.730
- Ø distance between 2 SNPs (n base-pairs): 51.500
- Amount of DNA needed:
  - eg. 1 ml blood contains > 2 µg
  - 1 dose of sperm contains ~ 200 µg
  - (10 roots of a hair contain ~ 50 µg)
  - ~ 1 µg)



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## Use in practical application

- Lab is an important part, BUT  
**SNP data has per se no information on ,traits‘**

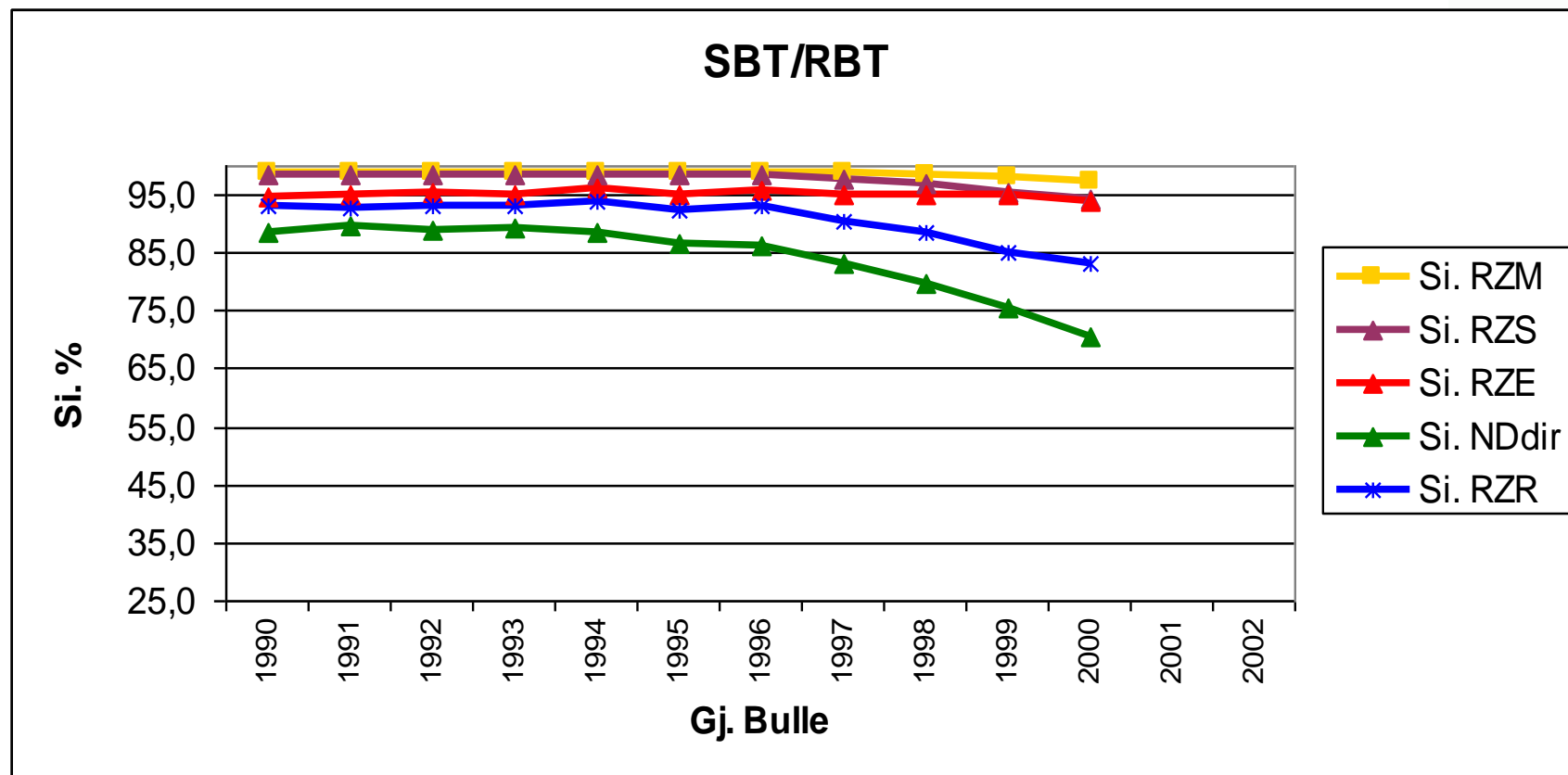
Steps:

- Genotype animals that have reliable EBVs from ,conventional‘ genetic evaluation
- Calculate regression formulas so that SNPs explain well the conventional EBV
- Use the regression formulas derived by historic data to evaluate young animals
- Select among these young animals





Available data,  $r^2$  for different traits eg in German Holsteins  
( $n = \sim 700, > 500$  daughters) → second crop bulls



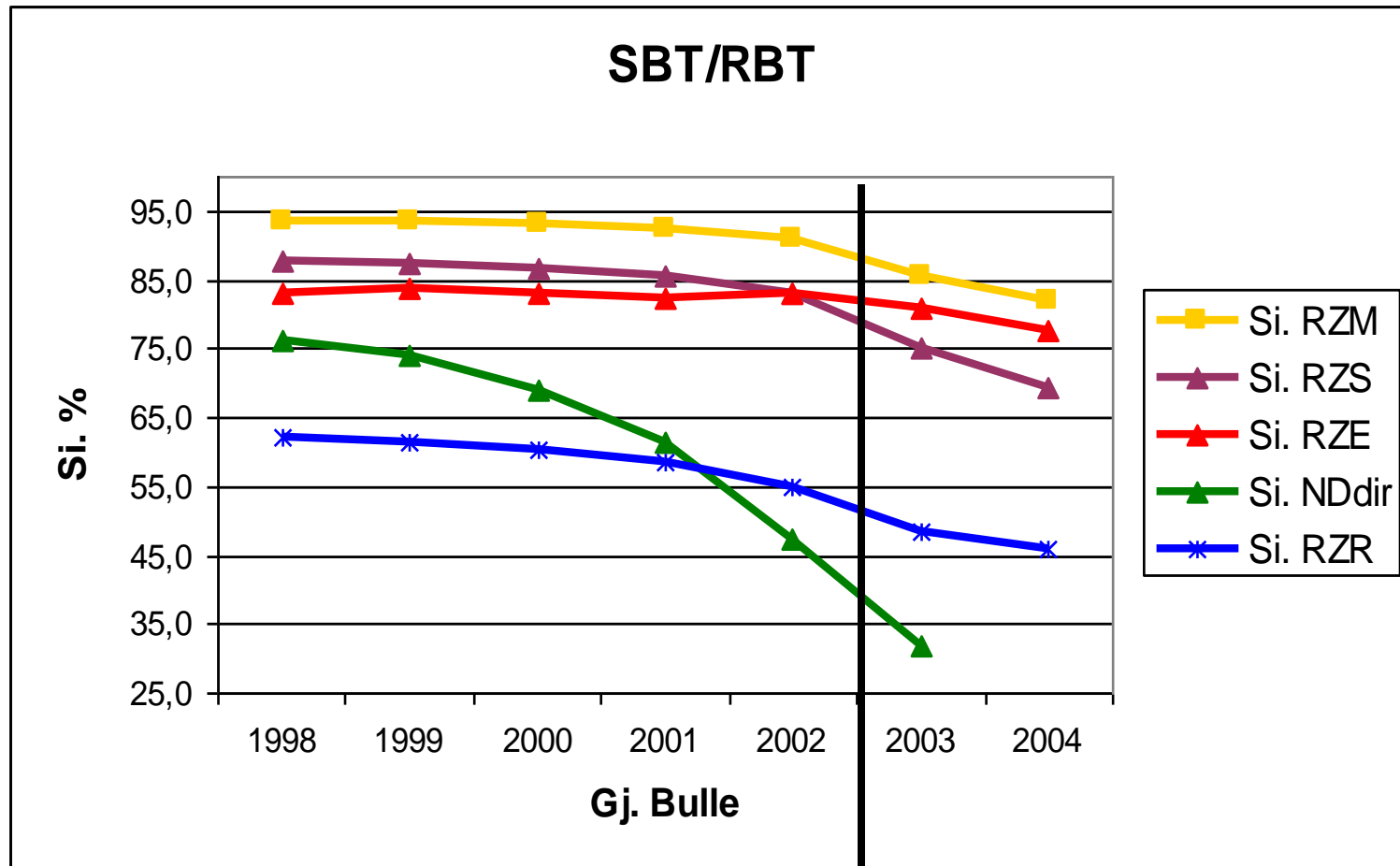
n WE-Bullen	126	130	100	101	91	77	77	101	72	46	16	1	
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# $R^2$ for progeny tested bulls German Holstein bulls (850/year) ca. 115 daughters per bull

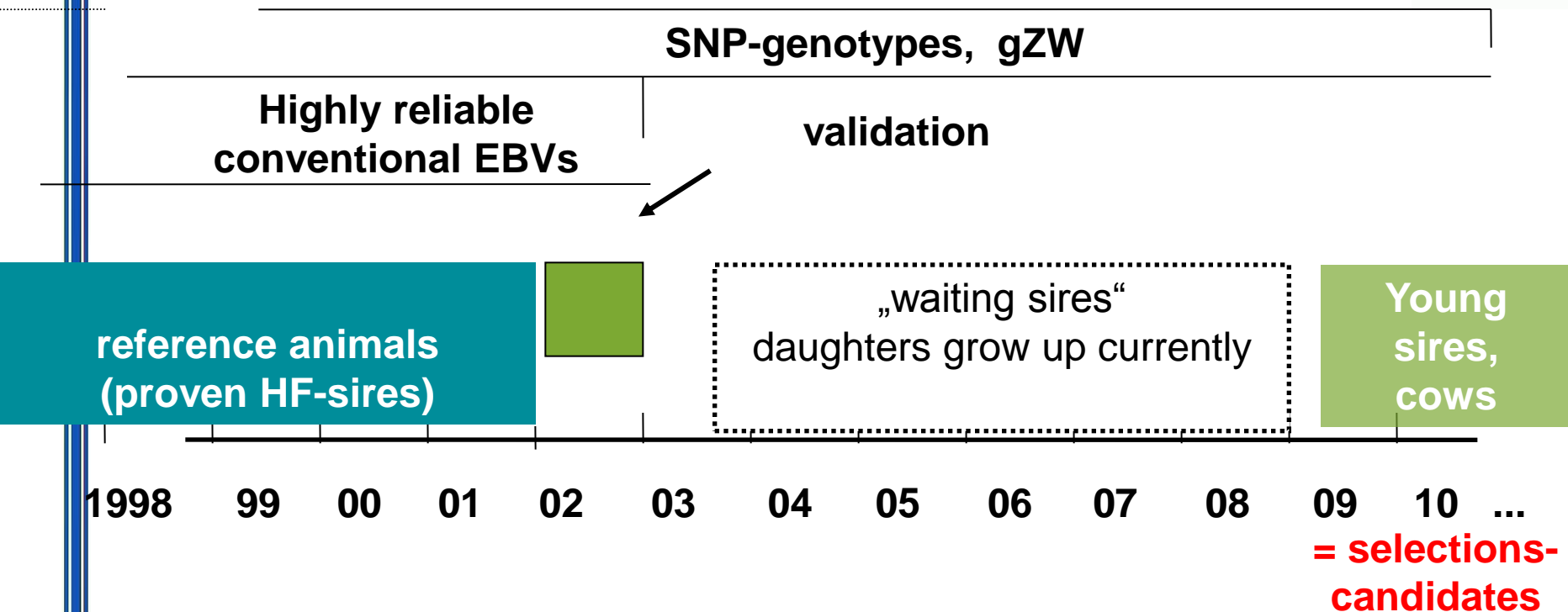


n M/S/E	829	853	872	1010	1014	847	62
n NDdir	829	853	872	1010	991	311	1





# Example for application – German Genotrack project; status quo 2009



- Estimation of SNP-effects: complete age-groups HF → 3500 sires
- Validation of SNP-effects:
  - Sires getting first progeny-based EBV in 2009 → ~ 900 sires
  - Strategy: correlation<sup>2</sup> between DGV: conventional EBV

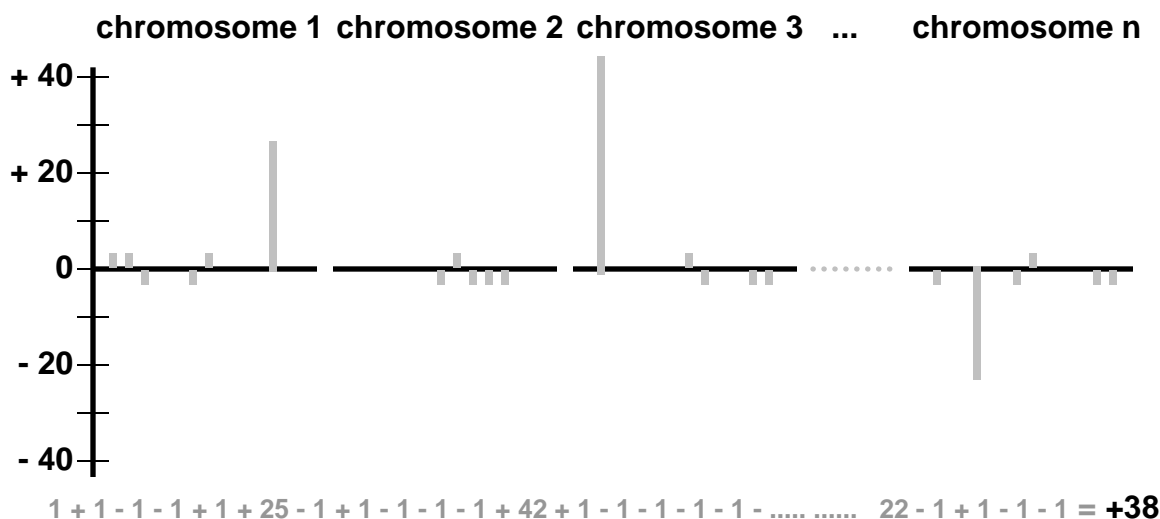




# Modell genomic evaluation – quality of results

- Quality of phenotypic data: conventional breeding value estimation  
→ Importance of conventional EBV
- Estimation of SNP-effects using „informative“ reference group
  - The more sires, the more accurate SNP-effects estimates
- Application of SNP-effects on young animals

SNP-  
effect  
(kg)



→ DGV



# Size of reference sample, van Raden, IB meeting, Jan 2009

Gain in reliability over PA in US



Bulls		Reliability Gain	
Predictor	Predicted	NM\$	27 trait avg
2130	261	13	17
2609	510	17	18
3576	1759	23	23
<b>947</b> 4422	2035	20	28
<b>1916</b> 6184	7330	31	30

Cows:





## Combination: conventional EBVs + genomic EBVs

conventional breeding value:

EBV / rel. (%)

Direct genomic value

DGV / rel. (%)

Index-theory

GEBV / rel. (%)

combined genomic breeding value

### Open questions:

- Realistic reliability of DGV ?
- If and how to combine DGV with conventional pedigree EBVs?

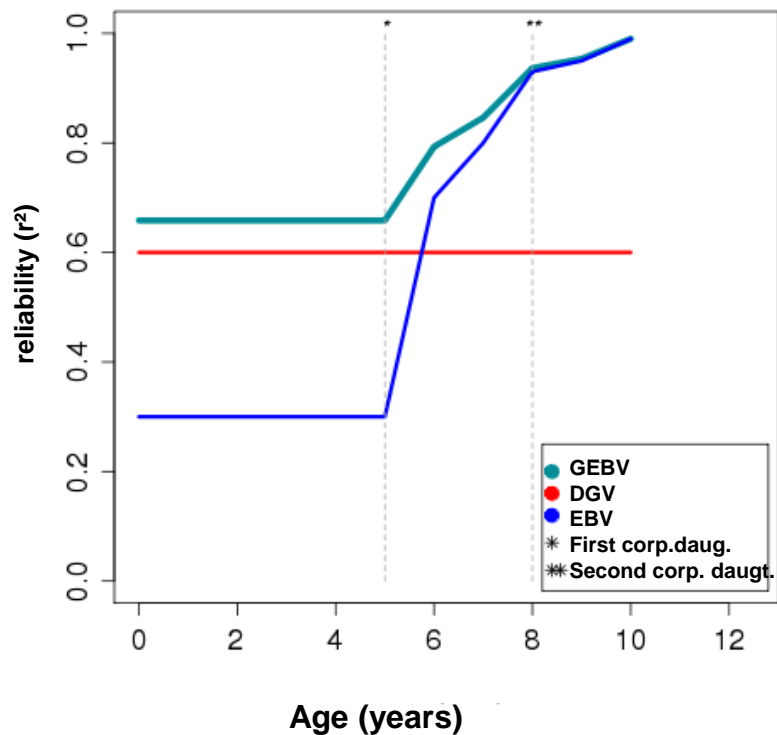




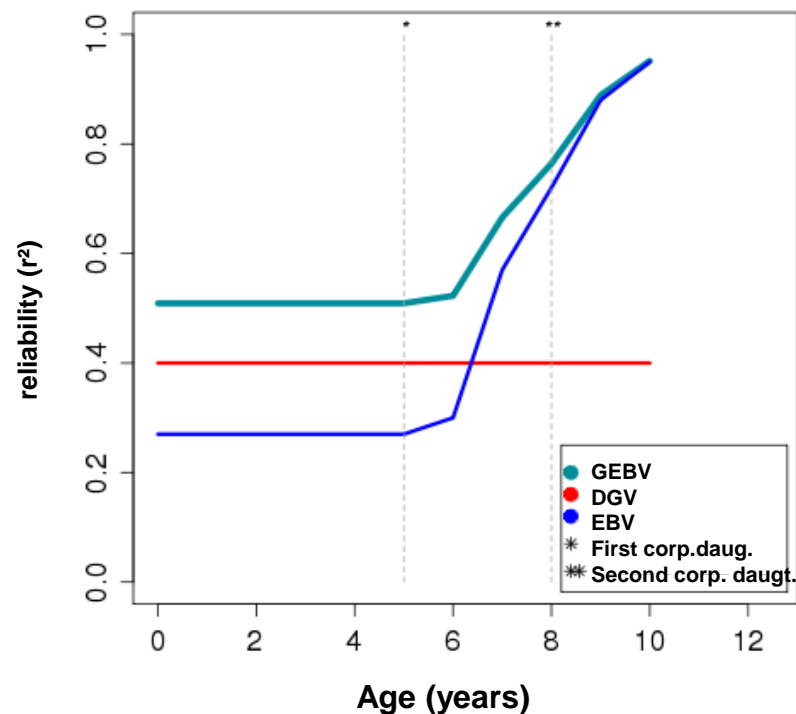
# Increase in reliability of the BVs for AI bulls



AI Bull Milk Yield

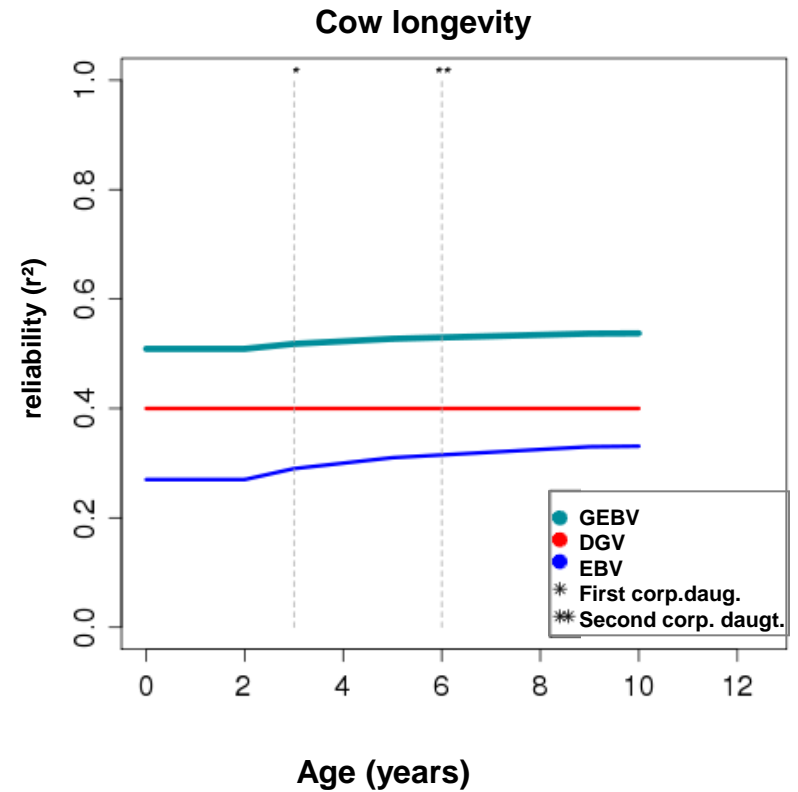
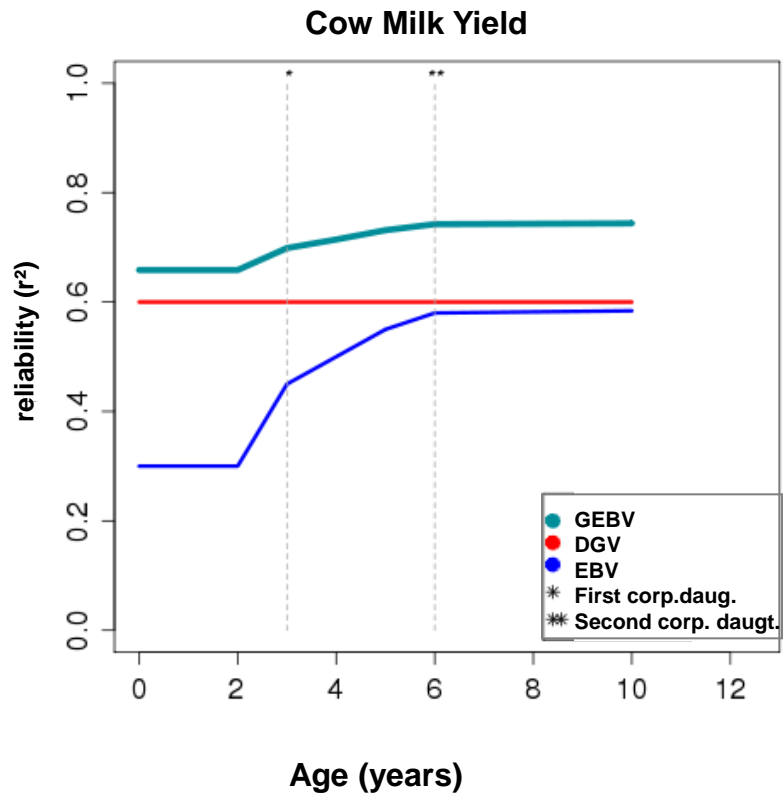


AI Bull longevity





# Increase in reliability of the BVs: cows





# Spectrum for practical application

1. Selection of young sires for A.I.
  - = selection of young sires based on GEBV
  - Conventional progeny test follows
2. Selection of bull dams
  - = selection & mating of bull dams based on DGV/GEBV
3. Selection of sires in A.I.
  - = selection of sires in A.I. based on GEBV
  - Sires age: 1-2 years, semen unlimited available
  - **Bulls without a progeny test → acceptance by farmers?**
  - **Increased use of natural service sires that do have a GEBV instead of AI bulls?**
4. ....







## Summary genomic evaluation

- **Genomic evaluation is a very useful additional tool, but it can only be used if**
  - Large amount of phenotypic data is collected on the traits of interest
  - Reliable pedigree information
  - Sophisticated conventional genomic evaluation
- **Potential of genomic evaluation can only be gathered if MORE phenotypic data is collected**
  - Functional traits (well defined eg by the ICAR WG ,Functional Traits‘)
  - New traits → e.g. composition of milk
- **Many options how to use this tool in breeding programmes have still to be examined**



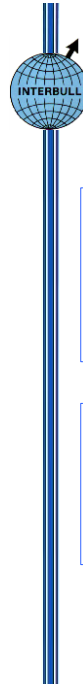
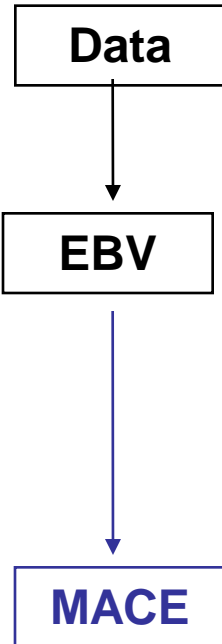


## International Comparisons

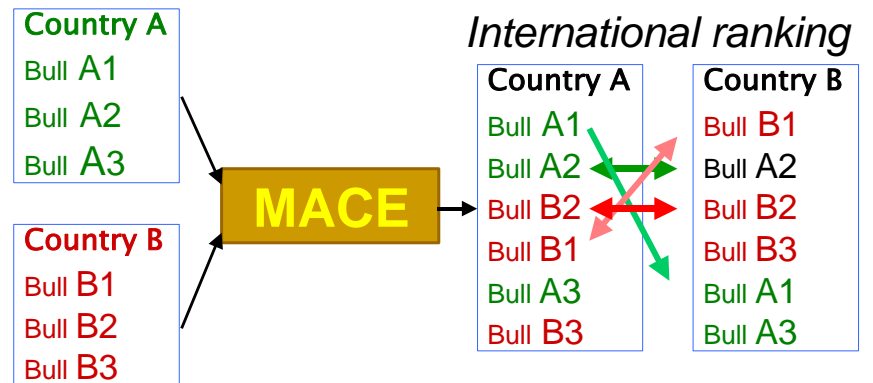
- **Status Quo (progeny tested bulls):**
  - BLUP national genetic evaluations
    - highly reliable EBVs (85-99%) for bulls with a **progeny test of 100-150 daughters**
  - BLUP national genetic evaluations
    - Transformation of these EBVs since 15 years via Interbull MACE  
→ **Bulls that are marketed worldwide**
- **Genomic evaluation**
  - Young bulls have reliabilities of 60-65%
    - ~10-15 daughters
    - GEBVs on the national scale
- **How to compare these bulls internationally?**



# MACE



## MACE visualised





## Interbull / ICAR meeting 27.1. - 30.1.2009



- Interbull workshop (27. - 28.1.2009, 101 participants)
  - Report Task Force (→ 7 experts from genetic evaluation centres)





## Results Interbull Workshop 27.1. - 28.1.2009

- Report Task Force Genomic Evaluation
  - Methodology works
  - but: assignment of an unbiased reliability measure for the genomic EBVs is not achieved yet → clear tendency to overestimate the  $r^2$ 
    - Approximation of  $r^2$ :  
use prediction formula for group of bulls with genotypes and conventional EBVs, but were **not** part of the reference population  
→ basis of validation procedure
- Urgent need for Interbull validation procedure
  - Genomic evaluation system → unbiased DGV and GEBV
  - Unbiased  $r^2$  for DGV and GEBV  
→ Both relevant for approval within EC
- Urgent need for Interbull services to transform GEBVs





# International Comparisons of GEBVs

## 1. Conversions via conversion formulas

- $GEBV_{import} = A + b \cdot GEBV_{export}$ 
  - Undesirable solution, large regression effect, no G\*E interaction considered

## 2. GMACE

- Like MACE, GEBV instead of EBVs
  - desirable solution, considerable regression effect, G\*E interaction considered

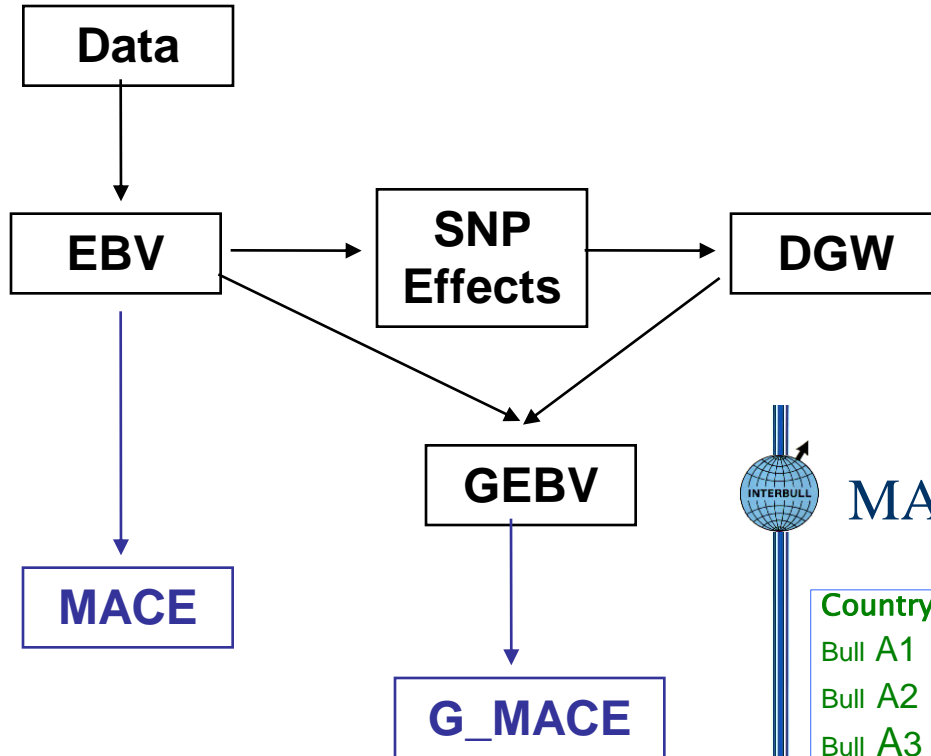
## 3. Use of importing countries formula

- Statistically best solution
  - Prerequisite: importing countries genetic evaluation unit allows incorporation of foreign genotypes

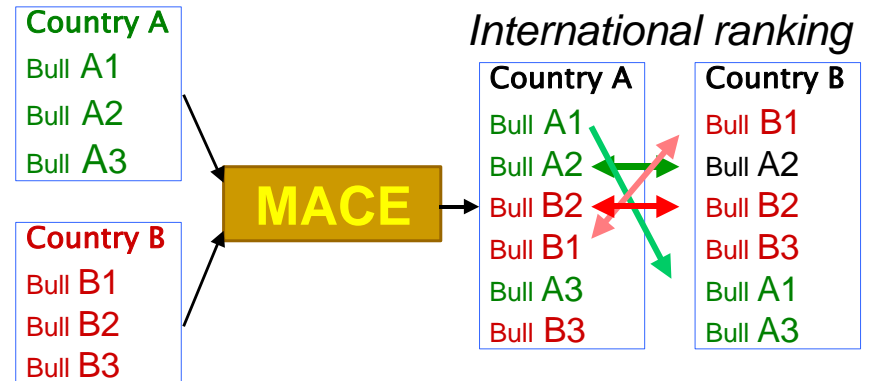
**1. and 2. can only be done within Interbull framework**

**3. Bilateral or within Interbull**

# MACE → GMACE



## MACE visualised





## Interbull Steering committee decisions



- Recognition of neutral, unbiased statistics from Interbull has to be maintained
  - Any recommendation for use of DGV/GEBV can only be granted after the validation test has been passed
- Validation test shall be developed by the IB Task Force until summer 2009
  - Approval at the Interbull Barcelona meeting in August 2009
- Steps for implementation
  - A) use of Interbull conversion formulas (summer/fall 2009)
  - B) GMACE (beginning of 2010)
  - C) develop a platform that allows exchange of SNP 0/1 data for pairs of countries (2010/2011)







## Summary



- Significant improvement of the methodology during the last 12 months
- Very successful meeting in Uppsala in January 2009
- Large breeding programmes want to cooperate in several areas
  - Improvement of the methodology
  - Sharing genotypes of the reference sample
- Small countries / populations seek implementation of the complete system within Interbull centre
- Interbull has made a strategic plan to introduce this new technology into its portfolio





**Thank you for your attention**