Final Report of Interbull's Pilot Study on International Genetic Evaluation of Female Fertility Traits

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SUMMARY

Female fertility data from 11 organizations/15 countries (including NAV) were used to estimate across country genetic correlations and international breeding values for all active bulls from these countries (including Denmark, Finland, Sweden). High genetic correlations and good connectedness among participating countries indicated that an international genetic evaluation at the Interbull level is feasible. Start of a new service by Interbull Centre for evaluation of female fertility traits was suggested and approved by the Interbull community. The first official test evaluation and routine evaluation are scheduled for September 2006 and February 2007. Results of this pilot study (Table 3) indicate that Nordic bulls are among the top 100 bulls in all country scales. This is just a confirmation that the breeding programs in the Nordic countries for the fertility traits have been very successful and have resulted in the production of bulls with the highest merit for these traits.

INTRODUCTION

Dairy cattle breeding is an international business, where elite sires are selected across country. This requires that the genetic merit of bulls can be compared across country for all traits of economic interest in order to achieve optimal genetic progress both locally and internationally.

Currently, international genetic evaluations (IGE) are being conducted for production, conformation, udder health, longevity, and calving traits by the Interbull Centre in Uppsala (Interbull, 2006). However, there are other traits of economic importance, which are not considered. Female fertility is one of them.

Female fertility is a trait of high economic importance. This is specially the case in Sweden and the other Nordic countries where broad selection criteria have been advocated for many years, but only recently have begun to gain international acceptance. Consequences of reduced fertility include prolonged lactations, reduced production per time interval, lower number of offspring per time interval, additional AI and veterinary costs, and increased involuntary culling. Furthermore, reduced fertility can be a sign of physiological problems for the cow, which can raise ethical concerns.

The reason for the lateness in implementation of an IGE for female fertility traits is attributed to the simple idea that female fertility is biologically so complex that no single measurement could reflect its entire complexity. This simple idea stems from the fact that the female animal (maiden heifer or cow) must go through a number of stages in every reproductive cycle. One way of classifying different stages of the reproductive cycle is as follows (for a different classification of the reproductive cycle see Van Doormaal et al., 2004):

For maiden heifer

- Demonstrating maturity and consequently heat;
- Conceiving after insemination(s);
- Carrying the calf to the term;

For cow

- Resisting fertility disorders after calving;
- Demonstrating heat after calving;
- Conceiving after insemination(s);
- Carrying the calf to the term;
- Repeating the cow cycle.

The biological complexity of female fertility (as shown above) can be summarized in five different abilities:

a) Ability to show maturity/heat;
b) Ability to conceive;
c) Ability to carrying the calf to the term;
d) Ability to resist fertility disorders; and
e) Ability to re-cycle.

One complicating factor that forces us to consider traits related to maiden heifers and cows separately is the moderate correlation between the same measurements in maiden heifers and cows. For example, Roxström et al. (2001) reported genetic correlation of about 0.7 for the same measurements in maiden heifer and cow.

Another complicating factor is the way different measurements are registered, i.e. as categorical variables (0 or 1 traits, shown in red in Figure 1) or as continuous variables (interval traits, shown in red in Figure 2).

Among the five abilities mentioned above it was deemed that there are very few countries with data on the onset of maturity in maiden heifers and heat in maiden heifers and cows. Further, it was deemed that the abilities to carry on to the term and resisting fertility disorders are, at least partially, covered by the Interbull international genetic evaluations for calving ease and stillbirth. Therefore it was decided to concentrate on the (b) and (e) above, i.e. the ability to conceive and the ability to recycle. Measurements used in different countries may pertain to only one of these abilities or to both.

There are potentially a large number of measurements that are related to the ability to conceive and to re-cycle. Some *simple measurements* are related only (or to a higher extent) to one of these abilities. For example conception rate (CR) is related to the ability to become pregnant, and the interval between calving and first insemination (CF) is related to the ability to re-cycle. However, some of the simple measurements can be put into a *combined measurement* related to the two abilities. Calving interval (CI) and days open (DO) are two examples of combining the two abilities in one measurement. There also exit *composite measurements* that are composite in the sense that they are linear (or otherwise any sort of) combination of other measurements, e.g. different fertility indices.

Today many countries have national genetic evaluations in place for different traits related to female fertility and more countries are expected to do so in the near future. There is a great need to harmonize evaluation methods and especially trait definitions as indicated above, but by considering female fertility at the international level this process could be stimulated. Genetic correlations were recently estimated among female fertility traits evaluated in the Nordic countries (Mark et al., 2001). These results were promising, but also showed that harmonization could lead to higher correlations. It would be desirable from a Swedish perspective if this work was carried out in Sweden to ensure that all the Swedish knowledge about female fertility is considered.

The Nordic countries have the most complete genetic evaluation systems for dairy cattle today, but we depend largely on non-Nordic countries for the selection of bulls, so we would like to get the international system as similar to ours as possible.

In the Holstein breed the majority of bull sires are of foreign (North American) origin, but there is no objective way of comparing Swedish sires with foreign sires without an IGE. Without an IGE the selection of bull sires will primarily be based on and limited to those traits, which are being considered in IGE, and not female fertility. For this reason and because there is an unfavorable genetic relationship between female fertility and production traits, there is currently an unfavorable genetic trend for female fertility for Holsteins.

Therefore, considering the two sorts of animals (maiden heifer and cow) and the two abilities (to conceive and to re-cycle) any individual country may have several measurements for female fertility. Given the low heritability values for fertility traits and the moderate correlations among measurements of each country, it seems prudent to consider the information from several measurements of each country simultaneously.

The method of evaluation used in Interbull international genetic evaluation (Interbull, 2006) is based on Schaeffer's (1994) the so-called Multiple Across Country Evaluation (MACE) in which different national genetic evaluations from different countries are considered to be different traits. However, because the residual correlations among the traits are assumed to be zero, only one trait per country can be handled in the model. Therefore, Schaffer's 1994 method has also been known as Single Trait MACE (ST-MACE). Later, Schaeffer (2001; see also Sullivan et al., 2005) introduced a new method which was capable of handling within country residual correlations and hence capable of inclusion of more than one trait from each country. This new method is commonly known as Multiple Trait MACE (MT-MACE).

Based on the arguments presented above, the aim of the Interbull pilot study for international genetic evaluation of female fertility traits was to implement the MT-MACE methodology for analysis of these traits.

MATERIAL

In the beginning of July 2004 initiation of the Interbull pilot study was announced. In the announcement, in addition to the explanation of points raised above in the Introduction, all Interbull member organizations were asked to submit data for the pilot study.

Data request also included information on the number and definition of desired traits to be submitted according to the following:

a) Traits that measure the animal's ability to become pregnant, i.e. high probability of conception. Two examples of traits for this ability are Non-Return Rate (NR) and Number of Inseminations (NI);
b) Traits that measure the animal's ability to re-cycle after calving. An example of a trait for this ability is the interval between Calving and First insemination (CF);
c) Traits that measure a combination of the above two abilities. Combination of the above two abilities might be through single measurements (e.g. Days Open (DO), Calving Interval (CI)), through index traits (e.g. Fertility Index (FI)), or through correlated composite traits (e.g. body Condition Score (CS).

For the purpose of the pilot study for fertility traits participating countries are invited to submit up to five (5) traits in following order:

1) One heifer trait related to the (a) above;

2) One cow trait related to the (b) above;
3) One cow trait related to the (a) above;
4) One heifer/cow related to the (c) above;
5) One heifer/cow related to the (c) above.

Deadline for submission of data was set to September 15th, 2004. However, because this was a pilot study, member countries were given some extra time. By November 2004 a total of 11 organizations, comprising 15 countries submitted data. Organizations/countries submitting data are shown in Table 1. Traits submitted by these 11 organizations / countries are also shown in Table 1.

METHODS

Input data were the results of national genetic evaluations (estimated breeding value (EBV) or predicted transmitting ability (PTA)) submitted by 11 evaluation centers with data from 15 countries. Trait definitions are shown in Table 1. Input data were transformed to PTA (where applicable) and standardized to a mean of 100 and standard deviation of 10 to be used in the consequent analyses.

Product moment (Pearson) and Calo-type correlations

At the outset product moment (Pearson) and Calo-type correlations were calculated for all 28 submitted traits. Editing criteria for choice of bulls (minimum of 20 common bulls born in the last 10 years of data, with a minimum reliability of 75%) followed the Interbull recommendations (Wickham and Philipsson, 1991).

ST-MACE correlations

Input data, which are the results of national genetic evaluations, are first subjected to within country de-regression and then used in a linear model containing country effect. Genetic groups are also used in the analyses. Simultaneous estimation of all correlations among the 28 submitted traits is computationally prohibitive. Therefore, country sub-setting of the data, as usually practiced in Interbull evaluations, was employed. In the beginning one trait from each of the 11 countries was included in each analysis until the 11-variate combinations were almost exhausted. There were 46 independent 11-variate analyses. Then, the countries with only one submitted trait were set aside and 7-variate combinations including one trait from each of the remaining seven countries were used until the minimum number of correlation estimates for any country/trait combination reached a minimum of 10 estimates. There were 45 independent 7-variate analyses. By doing so, for each country/trait combination between 10 and 55 separate and unique estimates were available. Bert Klei's MACE computer package (Klei, 2003, personal communication) was used for estimation of ST-MACE correlations.

MT-MACE correlations

The necessary modifications to current methodology available at the Interbull Centre were made. A multi-trait de-regressed weighting factor approach (Sullivan and Wilton, 2001) was used.

There were seven countries with multiple traits submitted for the Interbull pilot study. However, country reported parameters from CAN, Nordic countries (DFS), IRL and ISR indicated that all or parts of residual correlations were either zero or almost equivalent to the convergence criteria for estimation of correlations (i.e. 10^{-6}). Therefore, it was deemed that only country traits with a residual correlation larger than 10^{-3} need to be handled simultaneously.

The computational burden of estimating MT-MACE correlations is even higher. Consequently, national de-regressed proof files from 7-variate country/trait combinations including up to three traits from each country were used as input to a software package (Sullivan, 2005) in order to take care of non-zero residual correlations. There were 66 independent 7-variate analyses. Then, analyses continued with 5-variate combinations until there were enough correlations for all trait combinations. There were 111 independent 5-variate analyses. The resulting files were used again in Bert Klei's MACE computer package (Klei, 2003, personal communication) to estimate across country/trait genetic correlations.

Bending of non-positive definite correlation matrices

Because MACE correlations were estimated in sub-sets and accumulated in a 28x28 matrix, there was a need to bend the resulting correlation matrix. For this purpose the two methods of un-weighted and weighted bending (Jorjani et al., 2003) were used.

Estimation of international breeding values

Estimation of international breeding values followed the usual methodology used at the Interbull (employing Bert Klei's MACE computer package (Klei, 2003, personal communication)).

RESULTS & DISCUSSION

Product moment (Pearson) and Calo-type correlations

Product moment (Pearson) correlations between the two traits from ISR and other traits could not be estimated because they failed to fulfill the editing criteria. The remaining product moment correlations were generally positive and moderate to high. However, there existed many close to zero and also negative correlations. For example, non-return rate from GBR and age at first insemination from CAN had a correlation of -0.56. The Calo-type correlations were expectedly closer to unity (in either direction). Some of the within country Calo-type correlations were quite close to, or exactly equal to, unity, which raises two questions. The first question is related to multi-co-linearity and whether this may cause numerical instabilities for MT-MACE calculations or not. The second question, assuming a biological correlation of unity between the two traits, is related to the usefulness of having two measurements of the same thing. This second point seems like a dilemma and a paradox: we would like to have traits with high correlations, but not too high!

ST-MACE correlations

Obviously, ST-MACE correlations could not be estimated for within country traits because non-zero residual correlations would have been ignored under this methodology. Across country ST-MACE correlations were in general agreement with product moment and Calo-type correlations. The majority of these correlations were positive and moderate to high, which indicated the feasibility of international genetic evaluations for fertility traits. However, again there were a relatively large number of near zero and negative correlations. Given the trait definitions and nature of submitted measurements, presence of near zero or negative correlations came as no surprise.

Estimation of across country correlations with ST-MACE methodology is a time honored practice and there is no doubt in their usefulness. However, this was the first time that this methodology was used to estimate genetic correlations for such a diversely defined group of traits with such a wide range of genetic correlations. A common observation after application of ST-MACE methodology is small fluctuations of estimated genetic correlations depending on the data sub-setting. This phenomenon had been preciously observed under both country sub-setting and bull sub-setting (see for example Jorjani et al., 2005). In previous applications the fluctuations in correlations were rather negligible compared to the size of estimated correlations. In contrast, in the present study, the fluctuations could be as large as the size of the genetic correlation itself. One example pertains to the correlation between conception rate (CR) from FRA and calving to first insemination interval (CF) from CAN, both of which are legitimate fertility traits. Ten estimated correlations for this trait combination are -0.0408, -0.0462, -0.1002, -0.0217, 0.0555, -0.0343, -0.1001, -0.0384, -0.1038, 0.1390. It is evident that the fluctuations are at the same size as the estimated correlations and as the result the average of these 10 correlations is very close to zero. Another example depicted in Table 2 indicates the change of genetic correlations between daughter fertility from CAN and body condition score (CS) from IRL, which fluctuates between small positive and negative values depending on the presence or absence of other traits/countries in the analysis.

MT-MACE correlations

Kinds of fluctuations mentioned for ST-MACE correlations were are very pronounced in the MT-MACE estimated genetic correlations. The net result was that many country-trait combinations had average correlations which was very close to zero.

It is not clear why fluctuations are so large. At least three speculations come to mind. First, changes are the result of the REML procedure forcing the correlation matrix to be positive-definite. Second, there is a partial and/or semi-partial correlation structure among the traits that leads to the fluctuations. Third, these fluctuations are within the range of standard errors for the estimates and are nothing to be worried about. In any case, there are two consequences for the estimated correlations. The first consequence is that the number of near zero and negative correlations using MT-MACE are rather large. Mean of correlations are generally low and ranged from 0.02 to 0.61.

Further, comparison of means of correlations and mean of absolute value of correlations shows that for some traits all correlations have been positive (e.g. interval first-last insemination from DFS). However, for some other traits (e.g. age at first insemination from CAN) the mean of values (0.02) has increased to a higher value (0.20) for the mean of absolute values. This indicated a mixture of positive and negative correlations.

Bending of non-positive definite correlation matrices

Because the necessary correlations (e.g. 378 correlations for the MT-MACE model) were estimated in sub-sets, the collection of average correlations in a 28x28 matrix is most often non-positive definite and must be bended before it can be used in estimation of breeding values.

The bending process can be compared to a process of regressing all elements of a correlation matrix towards the mean of all elements. If the correlation matrix contains a mixture of positive and negative correlations and there are also a large number of near zero elements, then naturally a lot of correlations will get smaller after bending. The resulting positive-definite matrix contained has so many low correlations that it would have been meaningless to use them for estimation of international breeding values.

At this stage, the results were reported to Interbull's Steering Committee, Interbull Technical Committee and to countries participating in the female fertility traits pilot study. Consequently, a workshop was arranged (Wageningen, The Netherland, March 2-3, 2006) to discuss the results.

The outcome the Wageningen workshop was that more research on the subject of MT-MACE evaluation is needed and in the meanwhile the international community, including Interbull Centre, should move towards initiation of an international genetic evaluation for female fertility traits using ST-MACE methodology.

Estimation of international breeding values

Given the estimated across country genetic correlations by the ST-MACE methodology international genetic evaluations for estimation international breeding values/transmitting abilities were performed for 4 trait groups.

The 4 trait groups were related to the following abilities:

a) Traits that measure the animal's ability to become pregnant, i.e. high probability of conception. Two examples of traits for this ability are Non-Return Rate (NR) and Number of Inseminations (NI);
b) Traits that measure the animal's ability to re-cycle after calving. An example of a trait for this ability is the interval between Calving and First insemination (CF);
c) Traits that measure a combination of the above two abilities. Combination of the above two abilities might be through single measurements (e.g. Days Open (DO), Calving Interval (CI)).

Therefore, the trait groups were:

1) One heifer trait related to the (a) above;
2) One cow trait related to the (b) above;
3) One cow trait related to the (a) above;
4) One heifer/cow related to the (c) above.

Tables 3a-d will show the estimated correlations based on the above trait combinations. I each table there are also information on how many bulls from own country and how many countries were represented among the 100 hundred bulls in each country's scale.

CONCLUSIONS

Logistically it is feasible to use MT-MACE methodology. However, unless all correlations among the traits included in the analyses are high and positive, the results would not be well received by researchers and end users. Therefore, it is recommended that for the time being ST-MACE methodology for groups of similarly defined fertility traits to be implemented until the outstanding issues related to the MT-MACE methodology be resolved. Results of application of ST-MACE methodology are very encouraging. Estimated correlations for similarly defined traits are very high and the computational demand for performing an international genetic evaluation for female fertility traits are within limits of computational facilities available at the Interbull Centre.

Initiation of an international genetic evaluation of up to 5 female fertility trait groups is recommended.

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Reports of this project have been marked with an (*)

Table 1 – Submitted traits, their definitions, and their reported heritabilities

Country / Population	Trait name	Trait definition	h^2
Canada	NR	Non return rate at 56 days at first insemination, heifer	.020
	CF	Days between calving and first insemination, cow	.101
	NR	Non return rate at 56 days at first insemination, cow	.019
	AF	Age at first insemination (days)	.140
	DF	Daughter fertility (=65% NR_{cow} – 10% AF – 25 % CF)	.052
Austria, Germany	NR	Non return 90 days after 1st insemination	.020
Denmark, Finland, Sweden	NI	Number of AI's, heifer	.025
	CF	Days between calving and first insemination, cow	.042
	NI	Number of AI's, cow	.030
	FL	Days between first and last insemination, heifer	.020
	DO	Days open	.031
Spain	DO	Days open	.040
France	CR	Conception rate (success/failure)	.020
Great Britain	NR	Non return rate at 56 days	.018
	CI	Calving interval (days between 1st and 2nd calvings)	.033
	CS	Condition score (1=thin, 9=fat)	.237
Ireland	CI	Calving interval in lactation 1	.040
	CI	Calving interval across lactations (1-3)	.040
	CS	Body condition score	.240
Israel	CP	Percent conception per insemination	.015
	CR	Inverse of the number of inseminations to conception * 100	.020
The Netherlands	CF	Interval calving to first insemination (days)	.083
	NR	Non-return rate 56 days (binary trait)	.015
	CI	Calving interval (days)	.058
New Zealand	PM	PM21: presented for mating in first 21 days of mating period	.047
	CA	CAI: Cow bearing a calf in the herd's AI calving period	.020
	FI	Fertility index	.020
USA	DP	Daughter pregnancy rate (1% DP = 4 days in DO)	.040

Table 2 – An example of fluctuations in estimated correlation by the ST-MACE methodology

		CAN DF	DFS DO	GBR CS	IRL CS
CAN	DF	1.000	0.513	-0.073	**0.046**
DFS	DO		1.000	0.446	0.512
GBR	CS			1.000	0.918
IRL	CS				1.000
CAN	DF	1.000	0.488		**-0.093**
DFS	DO		1.000		0.502
GBR	CS				
IRL	CS				1.000
CAN	DF	1.000		-0.052	**0.130**
DFS	DO				
GBR	CS			1.000	0.914
IRL	CS				1.000

Table 3a: Estimated correlations for trait group 1: Heifer's ability to become pregnant

	CAN NR	DFS NI	FRA CR	GBR NR	ISR CR
CAN		0.73	0.62	0.83	0.83
DFS			0.49	0.58	0.42
FRA				0.52	0.43
GBR					0.93
ISR					
Top 100 bulls					
Own country	3	96	54	11	94
# countries	6	5	>6	5	3

Table 3b: Estimated correlations for trait group 2: Cow's ability to become pregnant

	CAN NR	DEA NR	DFS NI	FRA CR	ISR CR	NLD NR
CAN		0.90	0.82	0.79	0.92	0.94
DEA			0.73	0.93	0.83	0.79
DFS				0.73	0.86	0.82
FRA					0.80	0.71
ISR						0.94
NLD						
Top 100 bulls						
Own country	**4**	50	78	11	50	19
# countries	**>8**	8	6	9	>8	>8

Table 3c: Estimated correlations for trait group 3: Cow's ability to re-cycle

	CAN CF	DFS CF	NLD CF	NZL PM
CAN		0.95	0.92	0.49
DFS			0.98	0.56
NLD				0.65
NZL				
Top 100 bulls				
Own country	11	59	42	59
# countries	>6	7	>7	8

Table 3d: Estimated correlations for trait group 4: Cow's combined ability to become pregnant and re-cycle

	DFS DO	ESP DO	GBR CI	IRL CI	NLD CI	USA DP
DFS		0.89	0.93	0.77	0.94	0.91
ESP			0.90	0.82	0.89	0.92
GBR				0.90	0.96	0.86
IRL					0.83	0.79
NLD						0.91
USA						
Top 100 bulls						
Own country	48	0	4	3	40	26
# countries	>9	9	>9	9	>8	9

Figure 1 – Categorical measurements of fertility traits for non-return rate traits (28, 56 or 90 days), pregnant/non-pregnant or success/failure after each insemination.

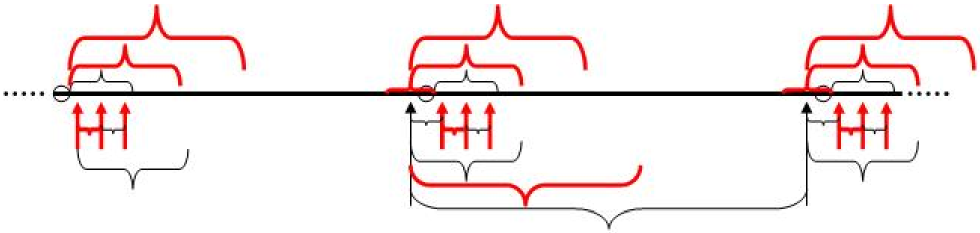

Figure 2 – Continuous measurement of fertility traits for interval first-last insemination, days open, calving interval.