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Synthesis Report: Animal Genetic Resources in the EU

During the last decades of the 20th century awareness about the need for conservation and sustainable use of Animal Genetic Resources started growing, in particular also in Europe. At global level, the adoption of the 1st State of the World's Animal Genetic Resources (FAO), and the Global Plan of Action for Animal Genetic Resources (FAO) were important milestones. European countries have been leading in this process, and there is a range policies and regulations at EU level that are related to, or support the agreements at global level.

Developments in society and technology have influenced the research agenda during the past decade. There has been an increasing focus on development and implementation of conservation strategies for farm animal genetic resources. Complementary in vivo and in vitro conservation strategies for animal genetic resources have been discussed in detail. Guidelines for in vivo and in vitro conservation of animal genetic resources have been developed by experts and FAO (FAO, 2012, 2013). These guidelines have global and European relevance and largely present the state of the art regarding conservation of farm animal genetic resources.

In the same period advances in molecular genetics have provided new opportunities for better characterization of breeds and for optimization of conservation and breeding strategies (FAO, 2011) While the use of micro-satellite markers was the standard in molecular characterization ten years ago, we are currently moving from high density SNP data to the use of whole genome sequence data.

In addition to literature on characterization and development of genetic tools for conservation and breeding, there are also several recent publications dealing with economic and non-genetic aspects of conservation and use of farm animal genetic resources. Promoting conservation through (sustainable) utilization is the key strategy, also illustrated by a number of animal genetic resources projects, funded by the EC Community Programme 2006-2011 (Commission, 2013).

The portfolio of scientific research projects and a variety of initiatives of actors in the Animal Genetic Resources domain clearly showed the value(s) of farm animal genetic resources, and the opportunities for increased use of underutilized breeds and marketing/valuation of their products

and services, for more effective and efficient conservation strategies, and for sustainable use of farm animal genetic resources.

The table below summarizes the outcome and impact of the main research areas.

Outcome and impact in the main research areas (AnGR)

Topic	Outcome and impact
AnGR in view of sustainable development	Awareness of AnGR functions and values; need for further characterization; in particular adaptive traits
Strategies for conservation and sustainable use	Guidelines and methods for complementary <i>in vivo</i> and <i>in vitro</i> strategies
Breed risk assessment	Extended and improved methods to support assessments of breed risk status
Valuation of breeds	Methods to determine market and non-market values
Environment and ecosystem services	Evidence about relationship between AnGR and environmental/ecosystem services
Prioritization for conservation	Extended methods for prioritization of breeds and individuals, including use of genomic data
High density SNP arrays and sequence data	Increasing amount of SNP and sequence data available as reference data, for breeding and conservation purposes
Characterization and breed evolutions	Better insight in breed history, introgression and selection
Genomics and conservation	Improved methods to monitor, to evaluate and to optimize within breed genetic diversity
Genomics and breeding	Accurate genomic prediction methods operational and implemented for major species and breeds
Gene bank collections	Increasing amount of genetic diversity in national gene bank collections and establishment of European network of gene banks (EUGENA)
Cryobiology and reproductive technology	Advances in cryopreservation protocols for different species and type of genetic material; prospects for cryopreservation of embryo's, ovarian tissue, testicular tissue, stem cells and somatic cells

Trends in animal genetic resources research

A number of topics were identified to describe the major trends in animal genetic resources research:

- Farm animal genetic diversity in view of sustainable development
- Strategies for conservation and sustainable use
- Breed risk assessment
- Prioritization for conservation
- Valuation of animal genetic resources
- Ecosystem services
- Whole genome sequencing

- Characterization and breed evolution
- Genetic diversity and inbreeding
- Genomics and inbreeding
- Genomics and conservation
- Gene bank collections
- Cryobiology and reproductive technologies

Farm animal genetic diversity in view of sustainable development

Animal genetic resources and farm animal genetic diversity are important in the context of global livestock sector development, climate change, sustainable diets, cultural heritage and biodiversity objectives. A number of publications cover one or several of these global challenges and highlight the importance of better characterization of farm animal genetic resources and improved conservation and management strategies (Baumung & Hoffmann, 2012; Godfray et al., 2010; I. Hoffmann, 2010; Irene Hoffmann, 2011; Seré, van der Zijpp, Persley, & Rege, 2008b). At global and European level there is a large diversity in livestock production systems, also requiring different breeding goals and breed types. In general there is a need for more strategic research to assist policy makers to make informed and strategic decisions related to animal breeding (Marshall, 2014).

Strategies for conservation and sustainable use

Recent global data that has been analysed by FAO for the 2nd State of the World's Animal Genetic Resources (FAO, to be published) show that 16% of mammalian breeds and 17 % of avian breeds have been classified as at risk, which is an increasing percentage compared to the 1st State of the World (2007). Moreover, 7% of the breeds is already extinct and a large proportion of breeds in the global database have no population data available. During the past decade it became generally accepted that in vivo and in vitro conservation strategies are complementary. FAO recently published guidelines for cryoconservation (FAO, 2012) and for in vivo conservation (FAO, 2013), reviewing the state of the art for these complementary strategies. Furthermore, a European group of experts presented a general framework to choose the most appropriate (in situ or ex situ) conservation strategy (Gustavo Gandini & Oldenbroek, 2007). For this purpose the use of a SWOT methodology to determine strategic directions also has an added value (Martin-Collado et al., 2013). Often there is a tension – within networks of breeders - between breed development and conservation goals (Lauvie et al., 2011).

Breed risk assessment

A variety of factors influence the risk status of breeds, in particular the effective population size of the active breeding population and the expected change in population size or threats to the breed. Risk categories (thresholds for number of breeding animals per breed) were recently revisited and discussed in detail. In the recently published in vivo guidelines (FAO, 2013) different risk categories and thresholds have been defined, between species with high reproductive capacity and species with

low reproductive capacity. This is because reproductive capacity influences the potential to recover from a decline in population size. Furthermore, geographical concentration can be an important risk factor in case of disease outbreaks (Alderson, 2009). The EURECA project funded by the European Commission, analysed in detail genetic and non-genetic factors to assess the (self)sustainability of breeds (Hiemstra et al., 2010).

Valuation of breeds

Breeds have different functions and values, which are relevant for prioritization of breeds for conservation and utilization. Recent work and methodology development has been done on valuation of breeds on the basis of market and non-market values. The total economic value (TEV) of a breed consists of the direct use value, indirect use value, option value, bequest value and existence value. A variety of case studies have been undertaken to determine or to estimate the different components of the total economic value. Several papers have been published recently, reviewing and explaining the methodologies in this area (Drucker, 2010; Zander et al., 2013), including introduction of the concept of Payments for Ecosystem Services (PACS) associated with market failures and the public good characteristics of agrobiodiversity conservation (Narloch et al., 2011).

Ecosystem services

The contribution of animal genetic resources to key agro-ecosystem functions such as nutrient cycling, seed dispersal and habitat maintenance is widely acknowledged (FAO Global Plan of Action for AnGR) (Jackson et al., 2007). Animal genetic resources and livestock management systems are integral parts of ecosystems and productive landscapes throughout the world. The Millennium Ecosystem Assessment (MEA) distinguished four groups of ecosystem services: provisioning services, regulating and habitat services, supporting services and cultural services. Livestock breeds are on one hand providers of ecosystem services and on the other hand dependent on ecosystem functions. Recently, some studies have been undertaken to collect information and evidence on the ecosystem services provided by livestock species and breeds (CGRFA, 2014, I. Hoffmann, Gandini, G., From, T., Hiemstra, S.J., 2014, Rosenthal, 2010).

Prioritization for conservation

There is a variety of technically sound methods and software available for prioritization of breeds for conservation, but application of these methods in practice is (still) limited (Boettcher et al., 2010). Recently, data integration on the basis of GIS has been introduced to integrate genetic, demographic and environmental factors (Joost et al., 2010). Next to this important development to integrate different data sources, an increasing amount of genomic data can be expected to support conservation decisions, within and between breeds. In this context, maximization of conserved genetic variation on the basis of neutral genetic variation only may not be sufficient to conserve breed-level variation in important traits (Hall et al., 2012).

High density SNP arrays and sequence data

Costs of genotyping individual animals have dropped sharply and enormous amounts of data have been generated during the past 5 years. SNP genotyping and sequencing technologies are developing very fast. With the development of bio-informatics and computing infrastructure this type of data can be used to genetically characterize animal genetic resources and to support and to optimize the conservation and sustainable use of animal genetic resources. Genomes have been sequenced and annotated for many species during the past decade, including for chicken, dog, cattle, horse, pig, sheep and rabbit (e.g. Dong et al., 2013; Elsik et al., 2009; Groenen et al., 2012; Qiu et al., 2012; Wade et al., 2009) and will become available for other species. Next generation sequencing (NGS) however has not fully exploded yet in the livestock sector. For some species many individuals have been fully sequenced already (Daetwyler et al., 2014). Most of the sequence data seems to be generated in cattle so far (Cantet et al., 2014). Besides better characterization of between breed diversity, whole genome sequence data and high density marker sets offer opportunities for genomic selection based on genome wide associations with relevant phenotypes. Moreover, it provides opportunities to better monitor or to assess the (potential) loss of rare alleles or haplotypes and to balance genetic improvement and long term conservation objectives.

Characterization and breed evolution

A large number of genetic diversity studies for different farm animal species, including through EU funded scientific research, have provided new insights in the long history of domestication, migration, selection and adaptation of farm animal genetic resources. The history of most of the farm animal species and breeds have been reconstructed (e.g. Ajmone-Marsan et al., 2010; L. F. Groeneveld et al., 2010; Miao et al., 2013). In particular studies of mitochondrial DNA genomes, which are maternally inherited, has helped to gain more insight in the origin and domestication of the species. The availability of high density SNP chips and full sequence information has further increased the understanding of domestication processes, breed characteristics, introgression, signatures of selection and adaptation mechanisms (e.g. Bosse, Megens, Frantz, et al., 2014; Bosse, Megens, Madsen, et al., 2014).

Genomics and conservation

In the past effective population sizes and inbreeding levels could be estimated only on the basis of pedigree data and/or using a limited number of markers. With the availability of sets of high density SNP markers or even whole genome sequence data, the variety of alleles, haplotypes and genotypes can be assessed more precisely (Allendorf et al., 2010; de Cara et al., 2011). Analysis of dense markers will give information about the level of heterozygosity, genetic diversity and signatures of selection.

Genomic selection has the potential to better manage within breed diversity and to limit inbreeding rates. Genomic data is being used to determine molecular coancestry, which is a more accurate indicator for inbreeding compared to pedigree based coancestry. The effectiveness of strategies to maintain within breed genetic diversity and to control the genetic background of a breed can be improved when genomic data is used (Toro et al., 2014). Relationship estimates on the basis of whole

genome sequence data are significantly different compared to estimates on the basis of high density SNP or pedigree data (Eynard et al., 2014).

Optimal contribution has become part of the regular animal breeding toolbox, balancing inbreeding control and genetic improvement. Sonesson and co-workers also showed that genomic information should be used both for estimating breeding values and for managing inbreeding, instead of pedigree-based inbreeding control (Sonesson et al., 2012).

Hinrichs and co-workers further contributed to a better understanding of inbreeding and inbreeding depressions, in particular the implications of natural selection and purging in influencing the magnitude of inbreeding depression. (Hinrichs et al., 2007).

Genomics and breeding

The availability of high density SNP chips was the start of methodology development for 'genomic selection' at the start of the 21st century. Higher densities of genetic markers (SNPs) and even the availability of whole genome sequence data is expected to further increase accuracy and impact of genomic selection. Accuracy of genomic selection using whole genome sequence data is expected to be slightly higher than using high density SNP chips. Analysis of whole genome sequence data is however more complicated.

Genome wide association studies will generate information about the size and distribution of gene effects that control quantitative genetic variation mutations and further about gene by gene and gene by environmental interactions. Besides genomic selection based on genome wide associations, there are also applications of whole genome sequencing in detecting monogenic deleterious mutations (Cantet et al., 2014). At the same time RNA sequencing is a relevant tool to measure overall or allele specific expression.

Much progress is made in development of methodologies for genomic evaluations. Recently, genomic selection has had an enormous impact on the livestock sector, starting with the dairy cattle sector. The key advantage of genomic selection is increased genetic gain through shortening of the generation interval, but investments are also high. Besides acceleration of genetic gain genomic selection also allows rapid discovery and elimination of genetic defects from livestock populations (Hayes et al., 2013).

Each livestock sector has to deal with very specific issues to apply and to benefit from genomic selection. When costs of genotyping will drop further, this will result in more marker based genetic evaluations. Possibly future focus will be more on inclusion of causal variants in the genetic model, instead of genome wide genomic selection only (Cantet et al., 2014).

Currently only large commercial breeding populations of widely used (international) breeds benefit from genomic selection. For breeds having smaller population sizes investments are usually too high to generate sufficiently large reference populations. Development of multi-breed reference populations and across breed genomic prediction might solve this problem, however predictions using information across breeds are complicated by the genetic distance between breeds (Lund et al., 2014). Predictions generally benefit from closely related individuals. On the other hand, genomic

selection may also provide opportunities for local breeds in the long run, when genetic analysis shows unique genetic variation or combinations of alleles that are not present in the more widely used breeds. Genomic introgression of specific genes or genetic variation (Odegard et al. Amador et al.) may provide new opportunities for better utilization of farm animal genetic diversity.

Although generating genomic data will become cheaper every year, it is as important to have sufficient and accurate phenotypic information. Phenotypic information remains the basis of animal breeding, New technologies can also contribute to accurate and high throughput phenotypic information.

Gene bank collections

During the past decade national gene bank collections for animal genetic resources have increased in size and relevance. It is technically possible to conserve a range of tissues/germplasm and species in cryobanks and recent developments in cryobiology and reproductive technologies has further increased the possibilities. On the other hand, there is a lot of variation in terms of technical and economical feasibility of establishing gene bank collections, between species and type of tissues/germplasm.

In Europe, the European Regional Focal Point on Animal Genetic Resources has taken the initiative to establish the European Genebank Network for Animal Genetic Resources (EUGENA) (Hiemstra et al., 2014). A uniform Gene Bank Documentation system (CryoWEB) has been developed for and is currently used by national gene banks (Duchev et al., 2010). Gene bank data in CryoWEB is connected to the European breed database (EFABIS). There is only few examples of assessment of collection diversity across countries (for example Danchin-Burge, Hiemstra, & Blackburn, 2011) showing that the three cryobanks have captured substantial amounts of genetic diversity for the HF compared with the current populations for Holstein in France, Netherlands and USA.

At global level, FAO published a set of guidelines for development and operation of national gene banks (FAO, 2012). One of the challenges of a gene bank is to establish collections of sufficient size, diversity and utility. Genetic tools and software are available to build and optimize gene bank collections (see for example review of (Boettcher et al., 2010)). At the same time – for different species and type of genetic material - there are technical, operational and budget constraints establishing gene bank collections. A number of recent studies looked into the costs of alternative strategies (G. Gandini et al., 2007; Silversides et al., 2012) which results can be used for decision making. Use of gene bank collections for scientific research or breeding/in situ conservation is growing but limited, in particular compared to plant genetic resources.

Cryobiology and reproduction

For most of the species cryopreservation and use of cryopreserved semen is technically feasible, but results substantially differ between species. For example results of inseminating ewes with frozen semen should be improved, and cryopreservation of semen of birds is generally less successful compared to mammals. The reproductive potential of tissues/germplasm stored in cryobanks is one of the key factors for successful cryopreservation strategies. The state of development in cryobiology

and reproductive technology has been reviewed in several papers in the past years (J. A. Long et al., 2014; Mara et al., 2013; Henri Woelders & Hiemstra, 2011; H. Woelders et al., 2012). Cryopreservation of semen is most common and generally easy to collect and to cryopreserve. However, cryopreservation of semen has the disadvantage that genetic diversity of female animals is not captured and re-establishment of a population through backcrossing using semen will take multiple generations. Recent research also shows alternative options cryopreserving different type of germplasm or genetic material for conservation purposes: embryo's, gonadic tissues, primordial germ cells, stem cells and somatic cells. For mammals cryopreservation of embryo's is an option, but also here differences between species. In general oocytes and embryos are more sensitive to chilling (Pereira & Marques, 2008). For birds it has been shown that ovarian tissue and testicular tissue can be cryopreserved and used for regenerating the targeted genotype after transplantation (Song & Silversides, 2007a, 2007b). Further improvements also have been made in cryopreservation of (peripheral blood) stem cell (transplants) (PBSCT) (Tijssen et al., 2008), and for cryoconservation of somatic cells a practicable and cheap procedure, in comparison to embryos or semen, was recently published (E. Groeneveld et al., 2008).

Implications for the conservation and use of animal genetic resources in the EU and globally

Recent and further advances in research and technology development (genetics, bio-informatics, reproductive technologies, socio-economic) can have a positive impact on conservation and sustainable use of animal genetic resources in Europe. The 'genomic revolution' offers great opportunities for characterization of animal genetic resources and rationalization of conservation strategies. Moreover, genomic selection is expected to further change the landscape in animal breeding and breed use. New technologies also make ex situ, in vitro conservation of animal genetic resources feasible for the majority of farm animal species and different types of germplasm or genetic material. There is a need and opportunity to further develop knowledge and technology for the purpose of AnGR conservation and sustainable use, and at the same time put more emphasis on implementation of methods and tools in practice.

The global shift towards specialized livestock production system and replacement of local breeds by cosmopolitan breeds has to a large extent already occurred in Europe. Complementary strategies are needed for conservation and sustainable use of AnGR, to maintain a broad range of AnGR to be able to deal with future uncertainties. Quality and scope of AnGR gene banks should be further enhanced to support in situ conservation and for long term conservation of farm animal genetic diversity. There is a need to further develop the concept of farm animal genetic resources as a public good for future generations. The EUGENA network will be an important vehicle in Europe to establish and develop a public gene bank or bio bank system in Europe for animal genetic resources. At the same time it is equally or even more important to manage and to monitor the long term sustainability of breeding programs, for local and for widely used breeds. Breeding organisations and networks of breeders should receive market- and society driven incentives to maintain and sustainably use their breeds.

Preparatory Action on EU Plant and Animal Genetic Resources

