Ministerie van Landbouw, Natuurbeheer en Visserij

Ministry of Agriculture, Nature Management and Fisheries

Executive Secretary
Convention on Biological Diversity
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Your letter of	your reference	our reference	date
		IZ. 2000/1746	14 December 2000
re:		extension no.	enclosures
Information on genetic resources. (TRC 2000/12095)		+31 70 3784934	3

With your letter dated 25 August 2000 you have invited the Netherlands to take specific actions following decision V/26 of the 5th Conference of the Parties to the Convention on Biological Diversity, related to the issue of access to genetic resources.

We believe this decision is a crucial step in the implementation of the Convention Biological Diversity, addressing a complex issue, of high relevance to sustainable use of biodiversity, and the equitable sharing of benefits arising out of the use genetic resources. The Netherlands therefore will fully implement this decision, for which we have started the necessary activities, in addition to those already in place, such as in the field of genetic resources for food and agriculture.

First, I can inform you that we are preparing an integrated policy document on genetic resources, which will reflect our objectives, programmes and activities in this field, directly related to the implementation of all our international obligations, in particular those set out in the framework of the CBD, FAO, WTO-TRIPS and UPOV. The paper will be prepared in co-operation between all relevant governmental department and with the involvement of major stakeholders in the Netherlands. Given the early stage of the policy process we are not in a position yet to present you any details of this policy plan.

You have already been informed of the nominations of our national authority, resting within the Department of International Affairs, and the national focal point for genetic resources, resting within the Centre for Genetic Resources of Plant Research International in Wageningen. Jointly, they have started a survey of genetic collections in the Netherlands, following the guidance provided by COP decision V/26. Given the high number of holders of such genetic resources in the Netherlands and the need for accuracy, we have not yet fully completed the survey. I have however herewith included three documents, which contains valuable information on our major genetic resources collections:

- scientific and economic aspects of genebanking in the Netherlands;
- legal and ethical aspects of genebanking in the Netherlands and
- Main trends and issues of genebanking in the Netherlands.

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If you would like to have further information on this documentation, I suggest you contact the national focal point, Mr. Bert Visser, who also stands ready to participate in the preparations for the follow up process in the framework of the CBD, leading to COP-6. I will send you additional information on genetic resources as soon as possible.

Finally, I would like to inform you that the Dutch government considers the issue of access genetic resources and benefit sharing a key priority for COP-6 CBD. We envisage that the Conference will be able to conclude upon a valuable package of a clear understanding of the key features of the issues and guidance for future work. As such we would very much like to see that COP-6 adopts, for example, guidelines on access to genetic resources and benefit sharing, which can both built upon and be further translated into more specific guidelines and agreements in the relevant sectors concerned, such as plant and animal genetic resources for food and agriculture, forest genetic resources, fish resources, and botanical and zoological gardens.

Rest assured that we have anticipated an active involvement on this matter within the CBD and other international fora and that we look forward continue co-operating with you and your staff.

Johan F. de Leeuw
Director-General
Ministry of Agriculture, Nature Management and Fisheries

Main trends and issues of genebanking in the Netherlands

Pattern of genetic resources collections

In the Netherlands, a relatively centralised approach and consequently the predominance of a few large key players has strongly influence the management of genetic resources. This picture holds in each of the four (plant, animal, microbial and human) domains.

In the plant domain, most public genetic resources collections for crops are maintained by the Centre for Genetic Resources, the Netherlands, under a mandate of the Netherlands Ministry of Agriculture, Nature Management and Fisheries. Concerning natural biodiversity, the Decentralised National Plant Collections under the Foundation of Dutch Botanical Gardens dominate the field. In both cases, large collections are well maintained, although funding limitations and problems are obvious and have become more aggravated over the years.
A conspicious feature of these collections is that these do not focus on diversity originating in the Netherlands, but that these are intended to cover the genetic diversity in the species, species complex, genus or plant family.

In the animal domain, a single collection holder, ID-Lelystad, is responsible for maintaing Dutch breeds which are threatened, in our major domestic species, like for CGN under a mandate of the Netherlands Ministry of Agriculture, Nature Management and Fisheries.
This activity started only recently and is still in its infancy, a feature of most European animal genetic resources collections. The private Foundation Genebank for Domestic Animals has been a track-blazer and continues to play an advisory role.

In the microbial domain, the CBS ('Central Bureau for Fungal Cultures') is the dominant player. As an institute of the Royal Netherlands Academy of Arts and Sciences it is financially supported by the Dutch government and holds a collection, covering representatives of virtually all fungal groups that can be cultured. In addition, CBS has been a depository for patent strains since 1955. The Netherlands Culture Collection of Bacteria which has combined collections of Delft and Utrecht, also comes under CBS. A large number of additional smaller collection holders is active in only this domain, which can be explained by the divergent applications or biological functions of the micro-organisms involved.

Finally, in the human domain, clinical genetic resources collections are maintained and further developed in a rapid pace, by the eight clinical genetic centres of the universities. The collection holders collaborate in the Society for Clinical Genetics the Netherlands and the National Platform for DNA diagnostics. The National Institute of Health and the Environment (RIVM) harbours a substantial collection of non-related individuals on the epidemics of chronic diseases, which has been established for research purposes.

Features of major collections are presented in Table 1.

Table 1. Features of major collections

Domain	Scope	Collection holder(s)	Collection size
Plant	Crops	CGN	21,000
	natural biodiversity	Botanical Gardens	>40,000
Animal	farm animals	ID-Lelystad/SGL	48/100,000*
Microbial	fungal species	CBS	35,000
	Bacteria	NCCB	6,000
Human	clinical samples	Clinical Genetic Centres	50,000 – 100,000
	epidemic research	RIVM	60,000

* number of breeds and samples respectively; planned size

An apparent feature of genetic resources management in the Netherlands is the modest role which is played by NGOs. A small number of NGOs is active in the plant and animal domain, mostly aiming at conserving traditinal crops varieties and animal breeds and promoting their utilization.

Large private sector collections are maintained as well, but these are generally not accessible fro third parties, often linked to research projects and not establisehd as long term diversity collections. These collections have not been described in this project. The size of these collections in the plant, animal and microbial domain is probably comparable to those in the public domain, whereas in the human domain the private sector does not play a significant role.

Collection ownership

Almost all collection holders regard themselves as the owners of the collections. In the microbial domain, except for CBS, awareness of the provisions of the CBD and its consequences appears to be low.
CGN does not claim ownership of its collections, in the light of the Convention on Biological Diversity and the international origin of large parts of its collections. CBS maintains collection materials of third parties, including under the Budapest Treaty. The Clinical Genetic Centres claim physical ownership on materials and associated information, but the source person retains the right to deny access to third parties or to request destruction of the materials and information.

Motives and objectives for collection building

Whereas CGN, the Botanical Gardens, ID-Lelystad and CBS explicitly state the conservation of genetic diversity as a major objective, this is not the case for most of the other collection holders. Research and breeding, healthcare and industrial applications form major motives for collection building, also for the collection holders which state the conservation of genetic diversity as a major objective. Whereas most collection holders utilize collection materials themselves, the four institutes mentioned above have a strong service role and mainly carry out resaerch on their collections to increase knwoledge and hence potential use of their collections.
In general, maintenance of collections is only regarded as warranted because of current or potential future utilization.

Most respondents anticipate an increase in size of their collections within the next five years, sometimes small and sometimes considerable. In only very few cases, germplasm has yet been discarded.

Quality measures

Quality control measures have been implemented at a larger scale and to a higher degree in the human and microbial domains. Quarantine and related regulations are generally respected. Safety back-ups have been established in a limited number of cases. Sometimes these are maintained as a duplicate collection by the same collection holder, sometimes at another site in the same location, and sometimes maintenance is the responsibility of another collection holder abroad. No general pattern emerges, although more attention for this aspect of collection management seems to be needed.

Data management

Computerization of data on the collection germplasm has been realized by all major collection holders, although some backlogs are reported due to constraints in human and financial resources. The collections of CGN and CBS, and of some botanical gardens can be directly

accessed through the Internet. This facility seems linked to the role these collection holders play as service institutions.

Access conditions and distribution frequencies

In the plant, animal and microbial domain collection materials are generally available for all users. For a long time, distibution and/or exchange of materials was organised on an informal basis. However, nowadays in these domains various conditions are posed on the distribution of materials. These conditions may concern intellectual property rights issues, embargo periods to protect the interest of the germplasm provider, limitations to research use, etc. Different conditions may apply for different germplasm, for different users and for different uses. All conditions relate to the potential commercialisation of the distributed germplasm or parts of it. Benefit sharing meachnisms have not been provided for in any of the access conditions. A considerable number of collections holders employs Material Transfer Agreements.

In the human domain, exchange or transfer of samples is rare, given the linkage to healthcare and the demographic nature of collections.

Financial management

Major collection holders mentioned in Table 1 receive allocated budgets for collection maintenance, or - at least - financial flows (tariffs) allowing for the building and maintenance of collections can be recognized (clinical genetic centres).
In most other cases, where collection management is an often modest side activity, collections are maintained from the overall budget of the collection unit or the larger administrative unit it forms part of.
Data on financial management generated by the questionnaire have remained extremely scarce. Generally, a poor insight seems to exist in the cost structure of collection management, i.e. the share of the total inputs spent on specific items.

Collaborative networks

In all domains collaborative networks play a major role. In the plant, animal and human domain these networks serve a crucial role to agree on division of tasks to avoid unjustified duplication of activities. Networks to be mentioned are the Society for Clinical Genetics the Netherlands, the National Platform for DNA diagnostics, the Decentralised National Plant Collections (all national), the European Cooperative Programme on Plant Genetic Resources Networks (ECP/GR), Botanical Gardens Conservation International, and the FAO Working Group on Animal Genetic Resources (international). CBS collaborates in the World Federation for Culture Collections (WFCC) and the Common Access to Biological Resources and Information (CABRI). Division of tasks seems to be a less prominent feature in the microbial domain, since no clear iondication on task division could be recognized.

Views on the European Union's role

The need for harmonisation at the EU or European level and the role for the European Union in that respect is met with considerable skepticism for various reasons.

In the plant domain, the establishment of European or international core collections and European or international crop databases has been reported.
However, physical centralisation is not regarded desirable for several reasons, including the need to regenerate, characterize and evaluate germplasm under the appropriate agro-ecological

conditions which vary widely over Europe, the need to serve users in their own language and from a limited geographical distance, the role of germplasm as bio-cultural heritage, and the related political desire to guarantee quality of maintenance and access to germplasm.

In the animal domain, veterinary and quarantine aspects limit options for centralisation of collections.

In the microbial domain, centralisation meets many reservations, and ideas on the major criteria for centralisation (by collection type, collection purpose, region or country) vary widely. Reservations include the risks in management at a single site, the need to link the collections to expertise on the germplasm, maintaining confidentiality on part of the germplasm involved, and guaranteed accessibility, linked to the collection site. Virtual centralisation (i.e.e to shared databases) and a central facility for back-up collections is suggested. Some respondents opt for a role in implementing the latter options.

In the human domain, little interest in European harmonisation seems to exist, mostly because these centres function within the national health care system and cross-boundary linkages concerning patient materials are limited. Similarly, a centralised facility to maintain collections appears irrelevant, given the primary role of the centres in health care and the patient-oriented sampling approach.

In conclusion, the need for harmonisation at the European level does clearly not extend to centralisation of collections, although a better system for back-up collections is regarded feasible by some of the respondents. Interest and scope exists for closer collaboration regarding other aspects of genetic resources collections management. Thus, initiatives for further harmonisation seem to be only relevant for the legal aspects (collection status, access conditions, intellectual property rights) and ethical aspects (privacy, benefit sharing) of genebanking in Europe.

LEGAL AND ETHICAL ASPECTS OF GENEBANKING IN THE NETHERLANDS: EMPIRICAL DATA

1. Introduction on methodology

Identification of collection holders

Identification of collection holders was based on the agreed criteria for inclusion in the project, i.e. the collections concerned should fit in the following profile:

- ex situ collections
- accessible to third parties
- systematically organised
- constituted with the aim to study or use or conserve genetic information
- consisting of living organisms or DNA or sources of DNA.

For identication of collection holders different approaches were taken for different domains.
For the plant domain substantial in-house knowledge was available at the Dutch partner organisation, the Centre for Genetic Resources, the Netherlands (CGN), part of Plant Research International and of Wageningen University and Research Centre (Wageningen UR). Additional information was obtained through the use of the project questionnaires. The following collection holders were distinguished: public sector genebanks, botanical gardens, private sector working collections, and civil sector conservation initiatives (NGOs).
For the animal domain, a list of breeding companies and civil sector foundations was established in close collaboration with the Wageningen UR animal science institute ID-Lelystad, which itself is maintaining animal genetic resources collections. The number of actors in the animal domain appeared to be considerably smaller than in the other domains. A similar distinction as in the plant domain was made between public, private and civil efforts to maintain genetic resources.
For the microbial domain, expertise within the plant protection unit of Plant Research International was used to establish a list of collection holders representing the entire microbial domain. Only public and private sectors were distinguished.
The human domain posed more difficulties. Firstly, it appeared more difficult to compose an overview of key players. Secondly, willingness to collaborate in this domain was most difficult to obtain. Two different types of activities and hence of collections could be distinguished in this domain, i.e. clinical genetics and anthropogenetics. Forensic collection holders were not covered as these were investigated by the Finnish team.
Table 1 provides data on the number of organisations identified and approached.

Many private parties responded by saying that none of their collections were available for third parties, and thus fall outside the realm of the study. However, as a result it seems that except for the human domain part of the picture is missed, i.e. no insight exists in the size and composition of collections in the private sector.
Although data from major players were obtained for each of the four domains, the total number of respondents has remained relatively low. Therefore, sufficient data were obtained to provide a typology on each of the four domains, but not extensive enough data to perform an elaborate data analysis.

Table 1. Number of organisations in the Netherlands approached and responding

Domain	Plant	Animal	Microbial	Human
Organisations approached	36	20	35	21
Organisations w/o accessible collections	10	16	7	2
Organisations responded	9	3	9	5
Percentage of response over approached and accessible collections	35	75	30	26

Data collecting process

The questionnaire was slightly adapted on language and ambiguities where perceived were removed. Also, two versions, one for the human domain and one for the other domains, were created to increase appropriateness for the human domain. The human version of the questionnaire was then once tested through an oral interview with one of the identified target organisations. Subsequently, the questionnaires were sent to the identified parties with an accompanying letter with the Eurogenbank letter head, to explain the objectives of the project and to ask for collaboration.
After five to six weeks, most parties that had not responded yet were contacted by telephone to enquire after their response. A substantial number of non-responding partners did not maintain collections that were available to third parties, and could be omitted from further analysis.
In few cases involving key organisations, an oral interview in stead of a response through the questionnaire was offered. In the case of the human and animal domain, an interim report was reviewed by key persons from this domain.
Response appeared to be as shown in Table 1.
In addition to the questionnaires and oral interviews annual reports, web site information and an EU survey on the status of "Genomes" research in the EU were used to compose an overview of the human sector, whereas project descriptions have been used for the overview of the animal sector.

2. Results

Typologies

Typology of the plant domain

Introduction
Plant breeding and seed production have traditionally formed a major economic activity in the Netherlands and continue to do so until this day. In this context, substantial collections of plant germplasm have been established in the private and public sector mainly, and to some extent in the civil sector. Many botanical gardens, often associated with universities, still reflect the Dutch colonial history.
Many Dutch breeding companies, now mostly owned by international agro-chemical agglomerates, maintain working collections as part of their breeding programmes. These collections have not been established for long-term conservation, are seldom accessible for third parties, and if so

under restrictive terms. Therefore, with a a single exception, these collections have not been included in this analysis.
Since 1986 the Dutch Ministry of Agriculture Nature Management and Fisheries has invested in the establishment of a central genebank, the Centre for Genetic Resources, the Netherlands (CGN), in Wageningen. After some initial years of independence CGN was merged with the then breeding institutes of the Ministry. These have now been privatised, and CGN is part of Plant Research International, but its collections have remained part of the public domain. Plant Research International currently employs over 700 staff.
A large reference collection is maintained by the Centre for Variety Research, the Netherlands (CVN), which is also part of Plant Research International. CVN carries out variety registration research and coordinates research in culture and use value for admisison to the national Variety List. This reference collection, partly maintained as seed and partly as plant material, contains approximately 700 ornamental varieties, and 3000 and 2100 horticultural and arable crop varieties respectively. The collection is not freely available for third parties.
Modest collections of trees (4000 plants belonging to 4 species) are maintained in the field by Alterra, the institute for Nature Management, belonging to Wageningen University and Research Centre.
The botanical gardens of several universities have coordinated their activities through the Foundation of Dutch Botanical Gardens (SNP). The SNP is responsible for the maintenance and supervision of living plant collections which together form the Decentralised National Plant Collection. This collection is maintained in 18 gardens.
Below, the legal status of the collections and collection holders, acquisition protocols, quality control and access conditions are discussed in more detail for major collection holders. Ethical aspects mainly regard the requirement of Prior Informed Consent in collecting germplasm, as well as aspects of benefit sharing on revenues stemming from the utilization of germplasm.

Collection status

All collection holders except CGN consider themselves as the legal owner of the collection germplasm.

CGN is part of Plant Research International B.V. which is a privatized, not-for-profit institution. According to its Material Transfer Agreement, CGN's collections come under the sovereign rights and jurisdiction of the state.

CGN, Plant Research International, nor other parties will claim ownership of the collections. This legal position is similar to the legal position of the collections of the CGIAR institutes, which are kept as in-trust collections under an agreement with FAO. It has to be stressed that the legal position of CGN's collections has not been formally agreed between the relevant parties, but can only be deduced from the text of the Material Transfer Agreement used by CGN. This is the more conspicious, since DLO has been privatized and does no longer form part of the Ministry of Agriculture, Nature Management and Fisheries. In conclusion, the status seems transparent but is not formally confirmed.
Some collections of CGN come under joint German-Dutch jurisdiction, in particular the collections of potato, sugarbeet and *Cichorium*. To this purpose the collection materials and necessary inputs for their management were shared. Each of the collection is maintained at a single location. The concept allows a more efficient collection management, and discussions have centered for some time on extension of this concept to other crops.

The reference collection of CVN, maintained to support variety registration research, contains materials which were obtained from breeders who have submitted a request to obtain plant breeder's rights, as well as samples which were obtained in the market. The former material remains the property of the breeder and is only maintained by CVN, whereas the later forms the property of CVN.

Acquisition protocols

Complementary to the MTA a Material Acquisition Agreement derived from the 'FAO International Code of Conduct for the Collection and Transfer of Plant Germplasm' and comparable contracts are used for international collection missions in which CGN participates. This has recently been the case for missions in Peru, Uzbhekistan and Kyrgizistan.

In general, such collecting misisons have become much more complicated to the point that they are probably discontinued until the negotiations on the revision of the FAO International Undertaking have been succesfully completed.

No Prior Informed Consent procedures have been applied in the case of collecting cultivated germplasm. Application of such procedures appears very complicated if not impossible in the case of acquisition of germplasm at local markets, a major source for traditional seeds, since the traders are not the developers of the germplasm and have often little knowledge of its background.

In the case of the botanical gardens, some materials are obtained through seizure of plant materials for which international trade has been forbidden according to the CITES treaty.

Quality control

In the case of CGN, phytosanitary requirements (EU Directives 97/46/EC, 95/44/EC and 77/93/EEC) are fully respected. No special insurances against liability sues of providers or users have been established.
No formal quality control system has been introduced by CGN sofar, but accreditation according to ISO 9000 is being prepared.

Access conditions

Germplasm in the CGN collections and accompanying information is made available to *bona fide* users under the conditions of a Material Transfer Agreement.

The Material Transfer Agreement (MTA) prohibits appropriation of the supplied germplasm by the receiver, and requests that users will make genetic information obtained over the germplasm available to the collection holder for further distribution, if needed after a limited embargo period of generally 3 years. The conditions for the germplasm itself also apply to the information accompanying the germplasm.
Germplasm samples are provided free of charge, and all information on the germplasm is accessible through the internet.

The major user group of botanical gardens has until now been formed by researchers and other botanical gardens. Therefore, distribution and exchange of materials (seeds or plant material) has long been arranged on an informal basis.

However, Material Transfer Agreements have now been introduced.

Introduction formed a response to conform to the provisions in the Convention on Biological Diversity, and given the increasing role of biotechnology in which the exploitation of plant diversity is not restricetd to crops and their relatives. These Material Transfer Agreements follow the model of Botanical Gardens Conservation International.

The civil sector, largely active in the maintenance and promotion of traditional crops and varieties, usually makes it materials available to all interested users, including indviduals.

Benefit sharing mechanisms

No provisions on benefit sharing mechanisms have yet been included in the MTA of CGN.

Such provisions are increasingly desirable because of the growing and changing utilization of the collections. Utilization takes three forms:

- direct cultivation and marketing of germplasm
- utilization of germplasm for traditional (i.e. non-GMO) breeding
- utilization of germplasm for the isolation of genes coding for or contributing to desirable traits.

Whereas IPRs on the first type of use is explicitly excluded on the basis of the signed MTA, utilization and subsequent protection by IPRs of the obtained products by plant breeder's rights and patents respectively is allowed.
However, since no national or international legislation has yet been established that would form the basis for benefit sharing provisions, the current MTA does not deal with the issue of benefiot sharing. One remaining option is only to explicitly state that

- the collection holder expects that benefits accrueing from the use of germplasm would be reported to the collection holder
- the collection holder is prepared to facilitate an agreement on benefit sharing between the user and the country of origin represented by its authorities.

Implementation of such arrangements would be very complicated and a generic benefit sharing mechanism would be much preferred.
Another remaining option would be to include a provision in the MTA stating thet IPRs resulting from the use of the germplasm will not restrict the utilization of the protected products in the country of origin, nor involve license fees from users in the country of origin.

Concluding remarks

Awareness of the provisions in the Convention on Biological Diversity regarding the conservation, exchange and utilization of plant germplasm, is generally very high in the public and private sector. This is less the case in the civil sector, but here germplasm involved often only relates to the national cultural heritage.

Typology of the animal domain

Introduction
Animal breeding in the Netherlands is a major economic activity, as demonstrated in the overview of the animal production sector. Substantial collections of sperm and embryos have been established as part of breeding programmes. However, none of these private collections are available for third parties, so these collections have been omitted from further analysis.
The only accessible collection has been established since 1993 by the Foundation Genebank for Domestic Animals (SGL). This initiative concerns a collection of five Dutch cattle races, conserved through 60,000 sperm doses. It was funded through private subsidies and a small starter subsidy of the Ministry of Agriculture, Nature Management and Fisheries and managed by Holland Genetics in Eindhoven. Partners in the Foundation are the Dutch Cattle Syndicate and Holland Genetics (private domain), together with the Foundation for Rare Animal Breeds. In 1999, this collection has been relocated due to EU veterinary requirements to the Institute for Animal Science and Health in Lelystad (ID-Lelystad). Recently, new initiatives have been undertaken to establish and maintain animal genetic resources collections in the public domain.
Significant living *ex situ* populations of domestic animals are known. The Foundation for Rare Animal Breeds is facilitating the maintenance of rare breeds. However, rare breeds are maintained as part of the production system or are owned by hobby breeders. No clear collections have been developed yet.

Collection status and acquisition protocols

The status of the newly established collections maintained by ID-Lelystad has not yet been clearly established.

One option is that like for CGN these collections will come under the sovereign rights and jurisdiction of the state. In that case ID-Lelystad nor other parties will claim ownership of the collections. The other option is that the collection will remain c.q. become the property of the SGL, under a written agreement with the Ministry of Agriculture, Nature Managmenet and Fisheries covering access conditions to the collections.
Sperm samples are obtained when these are acquired for breeding and other purposes by the breeders involved. One set is then transferred to the collections at ID-Lelystad and stored for

conservation and future use. The collections at ID-Lelystad thus serve also as a security back-up for the breeder's germplasm.

Quality control
Veterinary requirements (EU regulation/Directive 88/407, 90/429 and 92/65) will be fully respected. No special insurances against liability sues of providers or users have been established.
No formal quality control system has been introduced.

Access conditions
All bona fide users will have access to the collections maintained by ID-Lelystad.
In contrast to plant breeders, animal breeders make the germplasm available to the genebank at the start of the potential comercial life cycle of that germplasm. Plant breeders protect their valuable germplasm through plant breeder's rights and germplasm of commercial plant cultivars is usually only included in the plant collections afetr the commercial life cycle of the germplasm. Therefore, an embargo period of 20 years maximally on the collections in ID-Lelystad will be employed to secure the interests of the breeders who make sperm samples available. This is to guarantee that the original breeders can fully exploit the genetic properties of the germplasm made avialable.

Benefit sharing conditions
The mandate of the collections maintained by ID-Lelystad is limited to Dutch breeds. This mandate renders benefit sharing a relatively simple issue in terms of the number of players involved. In fact, the issue has been covered through the arrangement on access conditions.

Concluding remarks

Only a small number of players is involved. Activities are relatively recent. Several issues concerning ownesrhip, and access conditions have not yet been unambiguously clarified.

Typology of the microbial domain

Introduction

In the Netherlands, micro-organisms form the basis of major economic activities, including the dairy industry and other food processing and beverage industries (e.g. breweries) as described in the overview. Substantial collections of DNA and cell cultures have been established as part of research and development programmes, comprising a total of approximately 60, 000 samples in the 9 responding institutions (25% of our targets). Collections are mostly in the hands of 'profit' organisations, i.e. commercial companies (which generally did not respond), and these collections are not available for third parties. Moreover, university collections appear to be under-represented. Therefore, information on these collections remains elusive, and has not been included in the present analysis. The present data are mainly referring to 'research collections', i.e. the main activity of the present respondents concerns research rather than conservation.

Public and private collections show a large diversity in many aspects, and may therefore provide a reasonable, although slightly skewed impression of the total of collections in the microbial domain in the Netherlands as exemplified below.
In comparison with the plant and animal domain the management of microbial resources is much more scattered over a larger number of collection holders, which can be explained by the divergent applications or biological functions of the micro-organisms involved. The only large player in this area is the Central Bureau for Fungi (CBS), which was established in 1903 and now belongs to the Royal Academy of Sciences. It is also the only player for which the conservation of biodiversity is an explicit goal. The discussion on legal and ethical aspects is therefore strongly focussed on the CBS collections.

7 out 9 respondents are not aware of any national or international legal framework which is relevant for their activities.

Collection status

Collections are generally considered the property of the collection holders (CBS being an exception, see below). Ownership is generally not transferred (one exception).

From a legal perspective the collections maintained by CBS can be split into three groups. The largest section contains the collections which were establsihed by CBS itself for the purpose of research and conservation. A second section follows from its role as legal depository under the Budapest Treaty. A third section concerns a confidential safe deposit service.

The CBS has been a depository for patent strains since 1955. In the early years, deposition of strains was governed by national patent laws. In the seventies patent regulations became more internationalized, resulting in the establishment of the European Patent Convention (EPC). In 1978 the CBS was accepted by the European Patent Office (EPO) as a depository authority under this convention. In the eighties an additional, worldwide system came into being: the «Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purpose of Patent Procedures». As from October 1981, the CBS acquired the status of «International Depository Authority» (IDA) under the regulations of the Budapest Treaty for fungi, yeasts and Actinomycetes, since 1984 for bacteria other than Actinomycetes and since 1991 also for plasmids and phages.

The CBS offers a confidential safe deposit service for those valuable cultures for which patent protection has not been sought. Cultures will be stored as freeze-dried ampoules or frozen (below -130° C) and/or on agar. If requested, the culture can be transformed to a patent strain deposit at a later date.

Acquisition protocols

2 out of 9 respondents provide written information to germplasm owners before accepting new samples, and in no cases a Prior Informed Consent form is handled.
A good practice guideline is used in 4 out of 9 cases.

Quality control

Standard operating procedures (SOPs) have been implemented in all cases for storage, and in a majority of cases for viability testing and identity checks.
In only one case external auditing on collection management has been effected.

Access conditions

All collections are open to all requesters except in one case in which limitations have been set.

In a majority of cases, not all available information pertaining to the germplasm distributed is made available, and this confirms the information that in general limited information on acquired germplasm can be obtained from the supplier. Publications and electronic databases accessible though Internet sites are the major channels of distribution of information, followed by catalogues and patent applications. Sensitive information is protected either through confidentiality and company secrets, or through intellectual property rights (patents).

In four cases the use of Material Transfer Agreements was reported.

Further conditions to access may be set depending on the type of materials requested, the status of the receiving institute and the purpose of use. This includes conditions set by quarantaine requirements and permissions concerning the handling of pathogenic organisms.

Benefit sharing mechanisms

No benefit sharing mechanisms have been considered or implemented.

Concluding remarks

All collection holders favour harmonisation of legal and ethical frameworks at the EU level, and 7 out of 9 agree with agreements concerning the management of genetic stocks at the European level. Individual responses stress that this should not increase the regulatory burden.

Centralisation meets many reservations, and ideas on the major criteria for centralisation (by collection type, collection purpose, region or country) vary widely.

Reservations include the risks in management at a single site, the need to link the collections to expertise on the germplasm, maintaining confidentiality on part of the germplasm involved, and guaranteed accessibility, linked to the collection site. Virtual centralisation (i.e.e to shared databases) and a central facility for back-up collections is suggested. Some respondents opt for a role in implementing the latter options.

Typology of the human domain

Introduction

Two major areas can be distinguished, i.e. clinical genetics and epidemiological genetic research. The former actvity is directly linked to health care and is clearly the larger one of the two. Non-clinical, epidemiological research is carried out at a much smaller scale than clinical genetic research, and collections are smaller accordingly. Two examples of initiatives in the Netherlands concern a research project of TNO regarding multifactorial health problems of senior citizens, and a research project of the Erasmus University of Rotterdam studying the genetic make-up of a specific village population. Such collections may be regarded as working collections, since they function in the framework of temporary research projects.

In addition, The National Institute of Health and the Environment (RIVM) harbours a substantial collection of non-related individuals on the epidemics of chronic diseases, which has been established for research purposes.

In the Netherlands, clinical genetic research is carried out in eight centres, located in the eight medical faculties in the Netherlands. All centres belong to public universities. Private initiatives in clinical genetic research have not developed since only these eight centres have been recognised to supply services covered by health insurance. The clinical research in the centres serves primarily diagnosis of genetic defects, is patient-oriented and disease-specific. By consequence large collections of in particular cell lines and DNA samples have been established, but none of these collections have focussed on genetic diversity per se and research questions have not involved the genetic structure of populations. In other words, disease diagnosis forms the major purpose of collection building. In addition, in case of several hereditary diseases, families have been extensively searched for mutations and germplasm collections have evolved from this research. Approximately 80% of activities concern health care (diagnosis), the rest mainly research (linkage studies and contributions to diagnostic tool development). One of the laboratories acts as the forensic reference laboratory, but no long-term, collections based on forensic materials have been established.

Collection status and acquisition protocols

Physical ownership on materials and associated information is with the collection holders, but the source person retains the right to deny access to third parties or to request detruction of the materials and information.

For the collections of the clinical genetic centers, samples are obtained directly from patients, whereas sometimes individuals are recruited through patient organisations or the press. Patients are given information prior to taking samples and the introduction of Prior Informed Consent forms has occured or is being prepared. In several cases, the University Committee on Medical Ethics has been involved in monitoring procedures, in particular in relation to prior informed consent and privacy procedures.

Personal information is obtained including identity, family, and medical data. Sometimes the medical data are only accessible through the university medical centre departments treating the client, all samples being identified through patient number.

All data management has been computerised.

Quality control
In the case of the clinical genetic centres, accreditation to guarantee standard operation procedures has been obtained or is being prepared, and in addition visitation between the centres on quality standards has been implemented. At the centre in Leiden, Sterlab accreditation has been obtained in 1998 and since then all samples are analysed and stored in duplicate.
In general, no safety deposits in other locations have been established.
The collection activities of the RIVM have been certified based on ISO 9001.

Collaboration
Collaboration has been realised through the National Platform on DNA Diagnostics LOD.
Internationbal collaboration has been realised through the European Molecular Genetics Quality Network, in which the Dutch Clinical Genetic Centres play an active role.

Access conditions

Samples are not shared (e.g. divided) on a structural basis. When exchange occurs this is mostly accompanied by an informal letter confirming the exchange. In some cases, exchange involves foreign partners. Ownership is not passed on in case of exchange.

For instance, in the case of the centre in Leiden, materials are not exchanged with other institutions, and only researchers of LUMC are requested to analyse DNA samples, which have been anonymised. In exceptional cases, and solely on request and with consent of a patient, materials and/or information is transferred to a foreign institution, mainly to facilitate family analysis or further analysis of an expatriate patient.

Privacy arrangements
A national regulatory framework exists governing the operation of the centres, e.g. through legislation on management of patient materials.
The identity of individuals from which samples have been derived may be traceable, indirectly traceable or non-traceable, all these options occur.
A specific complication in the communication on heriditary diseases is the fact that the knowledge of being a carrier not only affects the individual analysed but also his or her partners and relatives. Counseling is being suggested as an important supportive task.

Benefit sharing mechanisms
In some cases, centres have been involved in patent applications, including as part of a defensive strategy inorder to keep technological applications available in the public domain. These patents may involve the use of specific DNA sequences for diagnostic purposes. No benefit sharing has been contemplated.

Concluding remarks
There is no national policy on the release of DNA sequence data or its ownership.

The sector shows a high awareness level concerning legal and ethical issues of genebanking, which is undoubtedly related to the health care profession of the collection holders.

The increasing role of the private biotechnology sector is expected to influence the functioning of the centres, but the pace and impact of these developments is yet unclear, and stakeholders in the centres take different positions towards such developments.

Little interest in European harmonisation seems to exist, mostly because these centres function within the national health care system and cross-boundary linkages concerning patient materials are limited.

Similarly, a centralised facility to maintain collections appears irrelevant, given the primary role of the centres in health care and the patient-oriented sampling approach.

Raw questionnaire data

Plant domain

Table 2. Ownership of the collections

Is the institution in charge of the collections also the owner of the collections ?	
Ownership	**Nr of answers**
yes, for all collections	7
yes, for part of the collections	2
no	1
Total	10

Table 3. Source of acquired germplasm

Modality of acquisition	Nr of answers
Direct field collection	5
Exchange with other collection holders	7
Advertising	2
Agreements with specified organisations providig material	2
Other methods	4
Blank	1

Table 4. Access conditions

Modality of access	**Nr of answers**
Access for all requesters	6
Conditions of access:	
Varies with collection	1
Varies with status of receiving institution	3
Varies with purpose of use	2
Only national	0
Agreement document used	3
Ownership transfer	1
Other	1
To data related to samples	2

Table 5. Cases of providing samples free of charge

Providing samples free of charge	**Nr of answers**
All cases (so far)	3
Academic institutions, fund.research	1
Education	1

In case of exchange	1
Private institutions	1
Members	1
Blank	3

Table 6. Information provideded with the distributed material

Type of information	Nr of answers
Passport data	5
Evalution data	5
Pedigree/genetic relationship data	2
Molecular data	1
User data	5
Other information	1
Blank	2

Table 7. Main partners in the exchange of genetic material

Kind of organisations	Nr of answers
Scientific research institutes	2
Other collection holders/ genebanks	5
Breeders	2
Other	2
blank/NR	2

Microbial domian

Table 8. Ownership of the collections

Is the institution in charge of the collections the owner of the collections ?	
Ownership	**Nr of answers**
yes, for all collections	6
yes, for part of the collections	2
no	
unknown	1
Total	9

Table 9. Source of acquired germplasm

Source of acquired germplasm	Nr of answers
Direct field collection	6
Exchange with other collection holders	5
Advertising	
Agreements with specified organisations providig material	1
Other methods	6

Table 10. Access conditions

Modalities of access	Nr of answers
Access for all requesters	8
Conditions of access:	
Varies with collection	3
Varies with status of receiving institution	5
Varies with purpose of use	5
Only national	0
Agreement document used	4
Ownership transfer	1
Other	7
To data related to samples	6

Table 11. Cases of providing samples free of charge

Providing samples free of charge	Nr of answers
All cases (so far)	0
Not usually	1
Academic institutions, fund.research	2
Education	0
Colleagues	1
Collaborative projects	5
In case of exchange	3

Table 12. Information provideded with the distributed material

Type of information	Nr of answers
Passport data	
Evalution data	2
Pedigree/genetic relationship data	1
Molecular data	4
User data	
Other information	2
Blank	3

Table 13. Main partners in the exchange of genetic material

Main exchange partners	Nr of answers
Universities	2
Scientific research institutes	5
Other collection holders/ genebanks	1
blank/NR	2

SCIENTIFIC AND ECONOMIC ASPECTS OF GENEBANKING IN THE NETHERLANDS: EMPIRICAL DATA

1. Introduction on methodology

Identification of collection holders

Identification of collection holders was based on the agreed criteria for inclusion in the project, i.e. the collections concerned should fit in the following profile:

- ex situ collections
- accessible to third parties
- systematically organised
- constituted with the aim to study or use or conserve genetic information
- consisting of living organisms or DNA or sources of DNA.

For identication of collection holders different approaches were taken for different domains.
For the plant domain substantial in-house knowledge was available at the Dutch partner organisation, the Centre for Genetic Resources, the Netherlands (CGN), part of Plant Research International and of Wageningen University and Research Centre (Wageningen UR). Additional information was obtained through the use of the project questionnaires. The following collection holders were distinguished: public sector genebanks, botanical gardens, private sector working collections, and civil sector conservation initiatives (NGOs).
For the animal domain, a list of breeding companies and civil sector foundations was established in close collaboration with the Wageningen UR animal science institute ID-Lelystad, which itself is maintaining animal genetic resources collections. The number of actors in the animal domain appeared to be considerably smaller than in the other domains. A similar distinction as in the plant domain was made between public, private and civil efforts to maintain genetic resources.
For the microbial domain, expertise within the plant protection unit of Plant Research International was used to establish a list of collection holders representing the entire microbial domain. Only public and private sectors were distinguished.
The human domain posed more difficulties. Firstly, it appeared more difficult to compose an overview of key players. Secondly, willingness to collaborate in this domain was most difficult to obtain. Two different types of activities and hence of collections could be distinguished in this domain, i.e. clinical genetics and anthropogenetics. Forensic collection holders were not covered as these were investigated by the Finnish team.
Table 1 provides data on the number of organisations identified and approached.

Many private parties responded by saying that none of their collections were available for third parties, and thus fall outside the realm of the study. However, as a result it seems that except for the human domain part of the picture is missed, i.e. no insight exists in the size and composition of collections in the private sector.
Although data from major players were obtained for each of the four domains, the total number of respondents has remained relatively low. Therefore, sufficient data were obtained to provide a typology on each of the four domains, but not extensive enough data to perform an elaborate data analysis.

Table 1. Number of organisations in the Netherlands approached and responding

Domain	Plant	Animal	microbial	Human
Organisations approached	36	20	35	21
Organisations w/o accessible collections	10	16	7	2
Organisations responded	9	3	9	5
Percentage of response over approached and accessible collections	35	75	30	26

Data collecting process

The questionnaire was slightly adapted on language and ambiguities where perceived were removed. Also, two versions, one for the human domain and one for the other domains, were created to increase appropriateness for the human domain. The human version of the questionnaire was then once tested through an oral interview with one of the identified target organisations. Subsequently, the questionnaires were sent to the identified parties with an accompanying letter with the Eurogenbank letter head, to explain the objectives of the project and to ask for collaboration.
After five to six weeks, most parties that had not responded yet were contacted by telephone to enquire after their response. A substantial number of non-responding partners did not maintain collections that were available to third parties, and could be omitted from further analysis.
In few cases involving key organisations, an oral interview in stead of a response through the questionnaire was offered. In the case of the human and animal domain, an interim report was reviewed by key persons from this domain.
Response appeared to be as shown in Table 1.
In addition to the questionnaires and oral interviews annual reports, web site information and an EU survey on the status of "Genomes" research in the EU were used to compose an overview of the human sector, whereas project descriptions have been used for the overview of the animal sector.

2. Results

Typologies

Typology of the plant domain

Introduction
Plant breeding and seed production have traditionally formed a major economic activity in the Netherlands and continue to do so until this day. In this context, substantial collections of plant germplasm have been established in the private and public sector mainly, and to some extent in the civil sector. Many botanical gardens, often associated with universities, still reflect the Dutch colonial history.
Many Dutch breeding companies, now mostly owned by international agro-chemical agglomerates, maintain working collections as part of their breeding programmes. These collections have not been established for long-term conservation, are seldom accessible for third parties, and if so under restrictive terms. Therefore, with a a single exception, these collections have not been included in this analysis. Total investments in maintenance of genetic resources by the private

sector, largely devoted at maintaining elite breeding lines, are estimated at 5% of total plant breeding efforts, and would amount to 1.1 – 2.2 million euro per year. The total size of private working collections is estimated at 50,000 – 100,000 lines.
Since 1986 the Dutch Ministry of Agriculture Nature Management and Fisheries has invested in the establishment of a central genebank, the Centre for Genetic Resources, the Netherlands (CGN), in Wageningen. After some initial years of independence CGN was merged with the then breeding institutes of the Ministry. These have now been privatised, and CGN is part of Plant Research International, but its collections have remained part of the public domain. Plant Research International currently employs over 700 staff.
A large reference collection is maintained by the Centre for Variety Research, the Netherlands (CVN), which is also part of Plant Research International. CVN carries out variety registration research and coordinates research in culture and use value for admisison to the national Variety List. This reference collection, partly maintained as seed and partly as plant material, contains approximately 700 ornamental varieties, and 3000 and 2100 horticultural and arable crop varieties respectively. The collection is not freely available for third parties. Part of the potato reference collection which was no longer needed by CVN has been transferred to a group of breeding companies which jointly maintains a field collection of 460 potato varieties with breeding value.
Modest collections of trees (4000 plants belonging to 4 species) are maintained in the field by Alterra, the institute for Nature Management, belonging to Wageningen University and Research Centre.
An apple collection, consisting of 85 traditional Dutch varieties and covering a wide genetic diversity, is maintained by the Fruit Research Station, which forms part of Wageningen UR.
The botanical gardens of several universities have coordinated their activities through the Foundation of Dutch Botanical Gardens (SNP). The SNP is responsible for the maintenance and supervision of living plant collections which together form the Decentralised National Plant Collection. This collection is maintained in 18 gardens. The collections serves a role in taxonomic and other research, as well as for chemical and molecular analyses and the distribution of starting materials for new ornamental crops.

Compared to other European countries, a relatively small number of NGOs is active in the management of plant genetic resources. These have strongly specialised on the maintenance and promotion of traditional varieties of arable crops and fruit trees.

Centre for Genetic Resources, the Netherlands

The Ministry of Agriculture, Nature Management and Fisheries has granted a yearly subsidy to Wageningen University and Research Centre of 1 million euro as part of its national genetic resources programme to maintain CGN's plant genetic resources collections and execute other tasks related to genebank management, such as documentation and information management, molecular characterization of germplasm and policy support. In addition, funding is secured through participation in several EU projects (100,000 – 200,000 euro/year), and in development oriented projects funded by donor organisations. Public-private collaboration takes form in service-in-kind by the breeding industry for characterisation and evaluation of collection germplasm. CGN employs a staff of 15 persons, excluding field staff.
Since its establishment, CGN - as an international latecomer - has focussed on strategies to optimise collection size and to optimize accessibility of information on the available collections. Furthermore, it focussed heavily on vegetable crops and potato, including germplasm from a wide geographic origin. Approximately half the budget (500,000 euros) is spent on collection management in a narrow sense, i.e. regenerating, characterizing, storing and distributing germplasm. Storage, testing of germination rates and distribution take a modest share of this budget, i.e. approximately 125,000 euros, whereas 200,000 euros are spent on regeneration field activities. The other half of the budget is spent on database management, documentation and information services, molecular characterization, promoting the utilization of the germplasm through collaboration with the private sector, policy support and international collaboration.
Current collection sizes of CGN are given in Table 2.

Table 2. Current CGN collections

Crop	Accessions	Crop	Accessions
Lettuce	2374	Wheat	5451
Tomato	1125	Barley	3436
Pepper	478	Oats	536
Eggplant	296	Maize	488
Cucumber	562	Peas	986
Spinach	382	Faba beans	726
Allium	300	Flax	568
Cruciferae	1680	Lolium and Poa	307
Potato	983	Clover	172

In addition a collection of wild relatives and old varieties of lily is being established.The share of wild relatives, landraces, obsolete varieties and research lines varies considerably per collection.

The total number of accessions in the collection is still slightly growing but a deliberate policy on stabilising the total size around 25,000 (now 21,000) has been formulated. The collections are not specifically focussed on originally Dutch germplasm, and on the contrary several try to cover global or regional genetic diversity in the crop. Given the upper limit to total collection size, maximization of the genetic diversity in the collection is the major target. Utilization of the collections for research and breeding is deemed highly important

Collections were founded on working collections from the former Wageningen breeding institutes, but have been expanded by gift, exchange and collecting missions, both national and international.
A database has been established which contains all passport and characterization data and which is on-line accessible (http://www.plant.wageningen-ur.nl/cgn).
Approximately 3000 samples are distributed per year, 50% to private companies and 50% to public users. 40% of the requests comes from users in other countries.
International databases for Brassica, lettuce and potato are being maintained.
Characterization (partly) and evaluation (fully) is carried out in close and formalised collaboration with breeding companies.
A molecular analysis using AFLPs and STMSs of CGN's entire lettuce collection has been carried out. Molecular characterization has also facilitated management of parts of CGN's wild potato collection, and of the flax collection. Molecular analysis has been used to confirm appropriateness of earlier management decisions concerning the bulking of Brassica landraces into single accessions, and to identify duplications and study the genetic relationships in the collections. Optimization of collection management protocols and the elaboration of the core collection concept form other major research efforts. Finally, bio-informatics, including strategies and approaches to store and retrieve large amounts of (molecular) data, have become an additional focus of CGN's research.

International exchange of plant germplasm, in particular uptake of germplasm in the CGN collections, has become increasingly difficult, due to constraints resulting from the interpretation of the Convention on Biological Diversity, which has come into force in 1994.
The result of the negotiations on a revision of the FAO International Undertaking will have a major impact on future international exchange.
Whereas international collaboration in the European region, mainly in the framework of the ECP/GR, has steadily become intensified, and several regional databases and core collections have been established, it seems currently unlikely that this collaboration will result in actual redistribution of germplasm accessions or collections and accompanying responsibilities at a large scale. Climatic differences and biological conditions throughout the European continent limit such concentration of conservation efforts to a considerable extent, in addition to political barriers to further integration.

NGOs
A number of NGO initiatives have been undertaken to maintain genetic resources.

However, the extent of these activities seems to be limited due to (1) the early and almost complete industrialisation of Dutch agriculture and the consequent loss of almost all traditional diversity, (2) the limited and late interest of the Dutch consumer in organic farming, and (3) the limited interest in traditional varieties.

Most conspicious NGOs are the Hof van Eden in Utrecht, maintaining a reported number of 30,000 poorly documented accessions from all over the world, a number of which are regenerated at a yearly basis to allow for adaptation; the Oerakker, maintaining several hundreds Dutch vegetable and cereal landraces in the field; and the Noordelijke Pomologische Vereniging, managing a partly decentralized *in vivo* apple and pear collection of traditional varieties. Each of these NGOs distribute (part of their) germplasm upon request, and promote the cultivation of traditional varieties.

Botanical gardens

The concept of Decentralised National Plant Collections was developed to acknowledge the linkages on expertise of the individual collections and university taxonomy departments, as well as the historical cultural values of each of the garden sites. The size of the total collections exceeds 40,000 plants.

Each of the gardens has specialised and duplication is being avoided. Most collections are based on taxonomic classification and consist of a single genus or family, but other collections are based on criteria like rock plants or bulbous plants. In addition, geographical criteria have been developed. For example, the garden in Leiden has specialised in SouthEast Asia, in Utrecht in South America and Wageningen in Africa.

The botanical gardens employ a total staff of approximately 130 persons including 20 academics, and they receive more than 600,000 visitors per year.
The budget of the decentralised collection in 1994 amounted approximately 1.7 million euro. Botanical gardens have recently encountered severe budget cuts from public sources, and many now operate on a (semi-)commercial basis. The Decentralised Collection receives funding from the private sector.

General observations

Regarding the status of the plant collections, 6 out of 10 collections are formally part of the private sector, but all but one operate on a not-for-profit basis.

In 7 cases the managing units come under a research organisation, the other respondents represent a breeding company and two NGOs.
The collection management units are small, most of them employ less than 10 staff, and none more than 50.

The size of the collections differs enormously, the botanical gardens and CGN harbouring large collections.

Four of the 10 collection holders report that the size is stable and that the collections are no longer growing or only to a very limited extent. In accordance with this observation, the same number of collection holders report to respect a maximum collection size, and to have discarded collection materials.

Conservation of biodiversity and research are identified objectives for seven of the respondents, and in general additional objectives are mentioned.

Regeneration, characterisation and evaluation are most often mentioned as activities of the collection holders, but many additional activities are carried out.

In a quantitative sense, inputs in evalution are considerably smaller than in conservation and characterization.

Only in two cases, the collection was not considered unique (alos available elsewhere). These collections may be characterised as working collections.
Decisions on acquisition are generally taken by the direct responsible units, involvement of central managers or boards being very limited. Exchange (7x), collecting and legal deposit agreements (each 3x) result in the acquisition of additional germplasm. Sources vary considerably. The origin and genotype of the germplasm, and anticipated traits each form major criteria for inclusion of

germplasm in the collections. This is in agreement with the reported purpose of acquisitions, i.e. increasing diversity, research and breeding, and as reference.
Passport data, evaluation data and user data (overlaps with evaluation data) is often obtained (each mentioned 5x) with uptake of new materials.
In seven cases storage is long-term, the other cases report shorter storage periods (< 10 years), either because plants do not survive, or because they loose value since new germplasm has been developed.

Only in four cases safety back-up collections appear to have been deposited elsewhere, lower than the number in the microbial domain if same-site duplication is included. In the cae of botanic garden and genebank, other botanic garden and genebanks provide back-up facilities, often on a mutual basis.
The number of distributed samples on a yearly basis varies greatly from 10 clones to several thousands of seed samples.

Information is made available through an electronic database in two cases only, publications being mentioned as the major means of information diffusion. This seems to be in contradiction with the reported eight cases in which a database is used for collection management. Apparently, this datbases is not always available to third parties. In addition, a reason might be that computerisation is reported to be partially in a number of cases.

Economic data are scarce and diverse, and give no insight in real management costs of the collections. In the majority of cases funding for the management of the collections comes from the overall budget of the organisation, explaining the very limited insight in cost structures.

Only 5 collection holders report which budget the had available in 1998. In no cases, payment is required for the distributed germplasm.

Financial contraints and the related lack of proper facilities is mentioned as a constraint and so is mentioned the interpretation of the CBD, as well as phytosanitary regulations.

Typology of the animal domain

Introduction
Animal breeding in the Netherlands is a major economic activity, as demonstrated in the overview of the animal production sector. Substantial collections of sperm and embryos have been established as part of breeding programmes. However, none of these private collections are available for third parties, so these collections have been omitted from further analysis.
The only accessible collection has been established since 1993 by the Foundation Genebank for Domestic Animals (SGL). This initiative concerns a collection of five Dutch cattle races, conserved through 60,000 sperm doses. It was funded through private subsidies and a small starter subsidy of the Ministry of Agriculture, Nature Management and Fisheries and managed by Holland Genetics in Eindhoven. Partners in the Foundation are the Dutch Cattle Syndicate and Holland Genetics (private domain), together with the Foundation for Rare Animal Breeds. In 1999, this collection has been relocated due to EU veterinary requirements to the Institute for Animal Science and Health in Lelystad (ID-Lelystad).Recently, new initiatives have been undertaken to establish and maintain animal genetic resources collections in the public domain.
Significant living *ex situ* populations of domestic animals are known. The Foundation for Rare Animal Breeds is facilitating the maintenance of rare breeds. However, rare breeds are maintained as part of the production system or are owned by hobby breeders. No clear collections have been developed yet.

Recent activities
The Ministry of Agriculture, Nature Management and Fisheries has granted a yearly subsidy to Wageningen University and Research Centre of 225,000 euro as part of its national genetic resources programme to establish novel animal genetic resources collections. These collections will be located at ID-Lelystad and daily management will be the responsibility of this research institute.

ID-Lelystad is part of the privatized Dutch agricultural research organization and employs a total of 650 staff members for zootechnical and veterinairy research and the execution of tasks as part of veterinary requirements. The department of Genetics and Reproduction is responsible for establishing and maintaining the genetic resources collections. A small staff of 3 fte takes care of major collection management activities, including processing of frozen material, sample management and database management, as well as national and international policy support. Major costs (> 90%) concern staff salaries.

Collection management

A workplan has been devised to establish exhaustive collections of Dutch races of horse, pig, chicken, sheep and goat between 2000 and 2004. These breeds include also all threatened Dutch breeds. This objective renders the collection unique. Table 1 presents the number of breeds and samples per species.

Table 3. Target numbers of animal breeds and samples in public collection

Species	**Number of races/breeding lines**	**Number of samples**
Cattle	5	60,000
Horse	4	2,000
Pig	12	24,000
Chicken	17	3,400
Sheep and goat	10	10,000

Collections will be updated yearly by uptake of germplasm from newly selected sires within these breeds.

A database is under construction, which will be directly linked to and feed into the FAO Domestic Animal Diversity System and the European Association for Animal Production. The database will contain information on pedigree and performance traits of individual animals.

New samples will be made available against no costs by breeders or breeding companies, whereas ID-Lelystad will serve as a back-up collections for its providers. The collection holder decides on uptake policy. Selection criteria include degree of endangerment and genetic uniqueness.

Samples are stored for an undetermined period, in agreement with long-term conservation objectives.

The following users of the SGL cattle collection can be distinguished: individual breeders and breeding associations, which have developed a breeding programme for a threatened population. Conditions to the use of the SGL collection include a contribution to the maintenance of a threatened population and the willingness to provide semen to the genebank of progeny born from genebank material.

Collection management is supported by research, in particular into cryopreservation methods and into optimal sampling strategies. Besides, breeding guidelines for small populations are developed. *In situ* conservation research takes an integrated approach and aims to explore the feasability to integrate animal genetic diversity in diversified agricultural production systems.

Germplasm in the collections and accompanying information will be available to *bona fide* users after an embargo period which is applied to protect the commercial interests of the suppliers of the germplasm, and under the conditions of a Material Transfer Agreement, yet to be concluded.

The Material Transfer Agreement will prohibit appropriation of the supplied germplasm by the receiver, and will request that users will make genetic information obtained over the germplasm available to the collection holder for further distribution.

Whether the current cattle collection, established by the Foundation Genebank for Domestic Animals, will require a new status has still to be determined. The above mentioned Foundation will advise the collection holder on policy and technical matters.

A major uncertainty regarding the future of the animal genetic resources bank concerns guarantees for funding and stability of funding levels. The Ministry of Agriculture, Nature Management and Fisheries has not been able to clarify the future funding position. In this context,

it has required a substantial contribution from the private sector to cover inputs allowing utilization of the collection germplasm.
Another uncertainty concerns the willingness of private partners to make their germplasm available to the genebank, even if a considerable embargo period is respected.

Typology of the microbial domain

Introduction

In the Netherlands, micro-organisms form the basis of major economic activities, including the dairy industry and other food processing and beverage industries (e.g. breweries) as described in the overview. Substantial collections of DNA and cell cultures have been established as part of research and development programmes, comprising a total of approximately 60, 000 samples in the 9 responding institutions (25% of our targets). Collections are mostly in the hands of 'profit' organisations, i.e. commercial companies (which generally did not respond), and these collections are not available for third parties. Moreover, university collections appear to be under-represented (see Table 4). Therefore, information on these collections remains elusive, and has not been included in the present analysis. The present data are mainly referring to 'research collections', i.e. the main activity of the present respondents concerns research rather than conservation.

Table 4. Distribution of questionnaire response over the total approached sample of microbial collection holders

	Profit	Non-Profit	
		University	Other Research Inst's
Total approached	9	18	8
Respondents	1	2	6

From several, both public and private collections, information could be obtained and included. These collections show a large diversity in many aspects, and may therefore provide a reasonable, slightly skewed impression of the total of collections in the microbial domain in the Netherlands as exemplified below.

In comparison with the plant and animal domain the management of microbial resources is much more scattered over a larger number of collection holders, which can be explained by the divergent applications or biological functions of the micro-organisms involved. The only large player in this area is the Central Bureau for Fungi (CBS), which was established in 1903 and now belongs to the Royal Academy of Sciences. It is also the only player for which the conservation of biodiversity is an explicit goal.

CBS

Originally, the CBS was a foundation supported by private means. In 1968 it became an institute of the Royal Netherlands Academy of Arts and Sciences which is financially supported by the Dutch Government, and has been assigned the joint role of management of the collection and scientific research.
The mission of CBS is to contribute to the knowledge of fungal biodiversity through the study of taxonomic and phylogenetic relationships, especially of filamentous fungi and yeasts, and to preserve cultures of living fungi of all kinds as a genetic resource available for research, reference and exploitation.
Over the years the CBS has extended its activities. Besides the maintenance of the collections and distribution of cultures, it now provides identification and research services for third parties. The CBS also offers consultancy, information services and training courses, drawing on the expertise of its specialists. The CBS is the Dutch node of the Microbial Information Network Europe (MINE), an EC sponsored international network to integrate and centralize data of the European culture collections.
Through relocation to Utrecht University it intends to strengthen its research capacities.

CBS' collection of living fungi is one of the largest in the world, covering representatives of virtually all fungal groups that can be cultured. The number of strains in the collection is well over 35,000, with an annual increase of approx. 1,000. In diversity of species it is unchallenged as a major reference centre for mycological research. The collection offers a unique resource for taxonomic research, and its performs this function worldwide through its character as a general service collection. Research in the collection itself is concentrated on preservation techniques, based on a thorough understanding of the physical and chemical conditions needed to ensure optimal survival after freeze-drying or deep-freezing.

An important feature is the good documentation associated with each strain. Database management to connect strain data with maintenance information and literature data is an area of special attention. On-line available information though six different databases ensures access to the strains in the collections.

Represented in its collections are the Ascomycetes (teleomorphs and anamorphs), which form the largest group of the fungal kingdom and by far the largest of those available in culture. Many groups contain representatives of great economic and medical importance. Ascomycete research will therefore be maintained as the central theme in CBS.
Another group is formed by the Basidiomycetes, in particular heterobasidiomycete yeasts and the Aphyllophorales. A third group is the Oomycetes. Particularly, species of *Pythium* and *Phytophthora* are of great economical/phytopathological importance. The number of specialists in this field is extremely small in the world.
In addition, CBS has been a depository for patent strains since 1955, and these activituies now fall under the Budapest Treaty.

General observations

The majority of the other respondents is located in research institutions in the private domain, but although part of the private domain, these mostly work on a non-profit basis. This pattern is reminiscent of that in the plant and animal domains.

Conservation of microbial diversity is an objective of only a subset of collection holders (3 out of 9 respondents), and conservation of biodiversity is not mentioned as the reason of requests for samples to third parties. However, in seeming contradiction with this is that 7 out of 9 collection holders state that criteria for uptake include whether a sample addes to the genetic diversity in the collection.

The top 3 of collection-purposes lists research (90%), reference (67%), and technical applications (56%). All collection holders except one mention research as a major, and in many cases the most important activity. The respondents as well as non-respondents holding microbial collections partly focus on more fundamental research, but in a majority of case, including in universities, applied research has the major focus.

Conservation and characterization, genetic studies, disease diagnostics and product development all form the areas of attention. The Plant Protection Service, which operates under a legal mandate and is responsible for quarantaine operations and the detection of plant pathogens, can be regarded as an exception, since it focuses mainly on diagnosis. The National Institute of Health and the Environment, ID-Lelystad and the National Animal Health Service all maintain human and animal pathogens respectively for both diagnosis and research. In accordance with these observations, the distribution of total investments over the different activities varies widely, and no clear tendencies can be observed regarding this issue.
In no cases an optimal collection size has been predetermined, and in a majority of cases (7 out of 9) germplasm once included is not discarded. All collection holders consider their collections as being unique. The average and maximal lengthh of conservation of germplasn is 20 and 50 years respectively. In 7 out of 9 cases collections have been duplicated elsewhere, including in the same institution.
All but one responding collection holders acquire new samples through their own collecting efforts, whereas exchange with other academic organisations and purchase are also practised by a majority of respondents. In three out of 9 cases samples were included because of legal deposit requirements. Limited and mostly molecular data seem to accompany new samples.
All institutes operate in an international network, indicating that the exchange of germplasm is likely to be international as well. Collaboration includes both the public and private sectors.

Very little information is provided about the maintenance costs of the collections. This can be explained either by unwillingness of the respondents to make such information public, but the alternative explanation that the maintenance costs and the cost items these consist of, are simply not known, is more likely given the fact that in all cases no separate budget for collection management had been created.

All collections are open to all requesters except in one case in which limitations have been set.

All but one collection holders have distributed germplasm in 1998, whereas the number of distributed samples varies greatly in accordance with collection size.
In a majority of cases, not all available information pertaining to the germplasm distributed is made available, and this confirms the information that in general limited information on acquired germplasm can be obtained from the supplier. Publications and electronic databases accessible though Internet sites are the major channels of distribution of information, followed by catalogues and patent applications.
Most databases of collections have been computerized to some extent (67%), and on average for seven years (some since as early as 1988) and with the use of commercial software (56%) or a combination of commercial and user-made software. Surprisingly, in 6 out of 9 cases not all information on individual samples appeared to be computerized, due to lack of funding and manpower.
In four cases the use of Material Transfer Agreements was reported. Further conditions to access may be set depending on the type of materials requested, depending on the status of the receiving institute and the purpose of use.
Handling fees are generally requested for processing and shipping of samples.

Development of preservation methods was indicated as a primary goal of future research. Indeed, loss of samples due to mortality is often mentioned as a problem.

Ownership is often indicated as unclear and/or poorly regulated.

No special insurances against liability sues of providers or users have been established. No formal quality control system has been introduced. Major problems include postal requirements, and unclear legal inhibitions. Access conditions have not been mentioned as problematic.

Most respondents anticipate a small but significant increase in size of their collections within the next five years. Uncertainties mentioned by most include problems with funding guarantees and availability of private collections.

Typology of the human domain

Introductory remark
Two major areas can be distinguished, i.e. clinical genetics and epidemiological genetic research. The former activity is directly linked to health care and is clearly the larger one of the two.

Epidemiological genetic research

Non-clinical, epidemiological research is carried out at a much smaller scale than clinical genetic research, and collections are smaller accordingly.

Two examples of initiatives in the Netherlands concern a research project of TNO regarding multifactorial health problems of senior citizens, and a research project of the Erasmus University of Rotterdam studying the genetic make-up of a specific village population. Such collections may be regarded as working collections, since they function in the framework of temporary research projects.
In addition, The National Institute of Health and the Environment (RIVM) harbours a substantial collection of non-related individuals on the epidemics of chronic diseases, which has been established for research purposes.
The size of the collections at the RIVM amounts to 60,000 DNA samples and 60,000 blood samples.

Samples are obtained by physical examination in population studies, which are based on randomly drawn individuals. Many of the characteristics mentioned below for the clinical centres apply. The work has been certified based on ISO 9001. The average storage length is reported to be 8 years, related to the research character of the collection. Exchange is only of the basis of formal agreements. In 1998 23,000 DNA samples and 23,000 blood samples were distributed. The collection has been duplicated at the IARC/WHO in Lyon.

Clinical genetic activities

In the Netherlands, clinical genetic research is carried out in eight centres, located in the eight medical faculties in the Netherlands. All centres belong to public universities.

Private initiatives in clinical genetic research have not developed since only these eight centres have been recognised to supply services covered by health insurance. The clinical research in the centres serves primarily diagnosis of genetic defects, is patient-oriented and disease-specific.

By consequence large collections of in particular cell lines and DNA samples have been established, but none of these collections have focussed on genetic diversity per se and research questions have not involved the genetic structure of populations. In other words, disease diagnosis forms the major purpose of collection building. In addition, in case of several hereditary diseases, families have been extensively searched for mutations and germplasm collections have evolved from this research. Approximately 80% of activities concern health care (diagnosis), the rest mainly research (linkage studies and contributions to diagnostic tool development).

Centres involved number between 50 and 200 staff members. In only few cases, specialist staff has been appointed for collection management. Usuually, collections are maintained from the overall budget available for running the centres. Only a small percentage of total staff time is specifically devoted to collection management. In most cases, no detailed insight exists in collection management costs. However, more detailed data were obtained in one case (the Leiden University Medical Centre), and given the similar set-up of the different eight clinical genetic centers in the Netherlands, these data may be regarded as representative. The costs to process a sample are approximately 500 euros. Net storage costs are small, and estimated at euro 0.18, 0.27 and 0.90 for DNA, cells and tissues, and cell lines respectively. The DNA diagnostics unit operates on a yearly budget of approximately 1.1 million euros. A standard tariff of 500 euros has been determined for all analysis, and this tariff is paid to the LUMC which provides the operating budget. This same tariff is also requested by all other clinical genetic centers in the Netherlands.

Collection management of Clinical Genetic Centers.

Samples are obtained directly from patients, whereas sometimes individuals are recruited through patient organisations or the press. Patients are given information prior to taking samples and the introduction of Prior Informed Consent forms has occured or is being prepared. Personal information is obtained including identity, family, and medical data. All data management has been computerised.

The number of samples obtained at a yearly basis has substantially increased over the last decade, given that gradually for more genetic defects diagnosistic tools have become available, and this yearly increment is expected to continue. In 1997, the clinical genetic centres jointly performed more than 14,500 diagnostic DNA analyses.

Collections are thus still growing, and few samples are discarded, mostly in cases that samples do not possess any specific characteristics or that these are unknown. No optimal collection size has been defined. Exchange of samples between centres is limited because of above-mentioned specialisation, but in some cases does occur. Samples are not shared (e.g. divided) on a structural basis. When exchange occurs this is mostly accompanied by an informal letter confirming the exchange. In exceptional cases, and solely on request and with consent of a patient, materials and/or information is transferred to a foreign institution, mainly to facilitate family analysis or further analysis of an expatriate patient. Ownership is not passed on in case of exchange. In some cases, exchange involves foreign partners.

Almost all data have been computerised.

Accreditation to guarantee standard operation procedures has been obtained or is being prepared, and in addition visitation between the centres on quality standards has been implemented.

No safety deposits in other locations have been established.

Sector organisation

The professional medical community is organised in the Society for Clinical Genetics the Netherlands. In addition, professionals meet through the National Platform for DNA diagnostics, which issues a periodical.

Agreements have been reached on the specialisation of each of the centres on a number of hereditory diseases, although some major diseases such as for breast/ovary carcinom are researched in most centres.

An overview of current DNA diagnostic research has been added as table 5, giving a clear indication of the type of hereditary diseases represented in the Dutch DNA diagnostic collections. A total of approximately 400 hereditary diseases can now be diagnosed through DNA analysis in the Netherlands.

International collaboration has been realised through the European Molecular Genetics Quality Network, in which the Dutch Clinical Genetic Centres play an active role.

Table 5. Hereditary diseases diagnosed in the Dutch Clinical Genetic Centres

Aarskog Syndrome
Achondro-Hypochondroplasia/Thanatophore dysplasia
Acute intermittant porfyria
ADCA
Adrenogenital Syndrome
Adrenoleukodystrophy
Agammaglobulinemia, X-linked
Alagille Syndrome
Albinism, X-linked (OAI)
Alport Syndrome
Amyloidotic polyneuropathy
Amyotrophic lateral sclerosis (SOD1)
Androgenreceptor-deficiency
Angelman Syndrome
Angioneurotic oedema
Aniridy
Antitrypsin-deficiency (alpha I)
Arylsulphatase A-pseudodeficiency
Ataxia Telangiectasia
Azoo/oligozoospermie (Y-deletions)
Bannayan-Zonana
Bartter Syndrome
Batten-Spielmeijer-Vogt
Beckwith-Wiedeman Syndrome
17-betahydroxysteroid dehydrogenase
Adrenohypolasia, congenital
Blackfan-Diamond Syndrome
BOR Syndrome (branchio-oto-renal dysplasia)
Breast cancer:
- BRCA1
- BRCA2

Brugada Syndrome Cadasil
Canavan, disease of
Cardiomyopathy, hypertrophic
Cardiomyopathy, dilated
Carnitine, palmitoyltransferase II deficiency
Carnitine-acylcarnitine deficiency
CBAVD
Central Areolar Dystrophy
Cerebrotendineuze xanthomatose
Charcot marie Tooth, disease of
Cholestase, progressive familial intrahepatic
Choroideremia (TCD)
Chronic Granulomatous Disease
Complex I-deficiency, autosomal recessive
Cowden, disease of
Craniosynostosis
CriglerNajjar, Syndrome of
Currarino, Trias of
Cystic Fibrosis
Cistathionine beta-synthase deficiency
Diabetes insipidus, central
Dihydropyrimidine dehydrogenase deficiency. (DPD)
Deafness, AR (DFNB1, connexin 26)
Deafness, type 9/diseaseof Meniere
Deafness, X-linked (DFN3)
DRPLA/HRS
Duchenne-Becker muscular dystrophy
EEC-Syndrome
Ehlers-Danlos Syndrome, type IV
Ehlers-Danlos Syndrome, type VII
Ellis-van Creveld Syndrome
Epidermolysis Bullosa, Dystrofic
Epidermolysis Bullosa, Junctional
Epidermolysis Bullosa, Simplex
Episodic ataxia, type I
Exostose, hereditary multiple
Facioscapulohumeral muscular dystrophy
FAMMM
Fanconi Anemia
Fish-eye disease
Fabry, disease of
FMTC
FRAXA
FRAXE
Friedreich Ataxia
Galactosemia
Gaucher, disease of
Gitelman Syndrome
Glaucoom (PAOG)
Glucocorticoid Remidiable Aldosteronism (GRA, hypertensia)
Glycerolkinase deficiency
Glycogen Accumulation Disease IA
Gorlin Syndrome
Hemochromatosis
Hemophilia A
Hemophilia B
Hemoglobinopthies
Hereditary spastic paraplegia
Cerebral Hemorrhage (HCHWA-D)
Hirschsprung, disease
HNPCC
Hunter, disease of
Huntington, disease of
Hurler, disease of (MPS1)

Hydrocephalus, X-linked
Hypercholesterolemia (familial)
Hyper IgD Syndrome
Hyperoxaluria
Hypertrofic cardiomyopathy
Hypodontia
Hypohydrotc Ectodermal Dysplasia
Ichthyosis, Lamellar
Ichtyosis, X-linked
Incontinentia Pigmenti
Kallman Syndrome
Kanalopathy (Natrium)
Kearns-Sayre Syndrome
Keratosis Follicularis Spinulosa Decalvans
Krabbe, disease of
LCHAD
Leber Heredirary Optic Neuropathy
Leigh Syndrome
Lesch Nyhan Syndrome
LiFraumeni Syndrome
Limbgirdle muscular dystrophy:

- LGMD2A (Calpainopathy)
- LGMD2C-F (Sarcoglycanopathies)

Long QT Syndrome
Lowe Syndrome
LPL deficiency
Lymfoproliferative Syndrome
Stomach cancer, hereditary (e-cadherene)
Marfan, Syndrome of
Markeranalysis
MASA Syndrome
MCAD
Mediterranean fever, familial
MELAS
Mendes-Da Cosa Syndrome
Meniere, disease of (autosomal dominant non-syndromal deafness)
Menkes, disease of
Metachromatic leukodystrophy
Methemoglobinemia
Methyleentetrahydrofolaat-reductase deficiency
Melavonaat kinase deficiency
Miller-Dieker Syndrome
Mitochondriële Myopathies
MODY type 2 and 3 (GK and HNF-1a)
Multiple Endocrine Neoplasia 1
Multiple Endocrine Neoplasia 2A
Multiple Endocrine Neoplasia 2B
Myoadenylate deficiency
Myofosforylase deficiency/McArdle's Syndrome
Myotone Dystrophy
Night blindness, Stationary Cong
Nail Patella Syndrome
Nance Horan Syndrome
Nefrogene Diabetes Insipidus (NDI)
Nephroneptisis
Neurofibromatosis, type I
Neuronale Ceroid Lipofuscinosis
Norrie, disease of
Nijmegen Fracture Syndrome
Oculo-Pharyngeal Muscular Dystrophy
OTC-deficiency
Osteogenesia Imperfecta (all types)
Papillary kidney cell carcinome, hereditary
Paragangliomas, hereditary form
PKU
Pelizaeus Merzbacher, disease of
Pendred Syndrome
Peutz Jeghers
Pick, disease of
Polycystous kidney disease (AD+AR PKD)
Polyposis coli, familial adenomatous
Polyposis coli, juvenil (PTEN)
Pompe, disease of
Porphyria Variegate
Prder-Willi Syndrome
Properdine deficiency
Progressive cone-dystrophy, X-linked
Pyruvate dehydrogenase complex I deficiency (PDHC deficiency.)
Pyruvate kinase deficiency
Renal Coloboom Syndrome
Renal Tubular Acidosis with deafness
Rendu Osler Weber
Retinitis Pigmentosa, X-linked + AR
Retinoblastoma
Retinoschisis, X-linked
RETT-Syndrome
Sanfilippo A, Syndrome of (MPSIIA)
SBMS (disease of Kennedy)
SCAD-deficiency (short-chain acyl-Coa dehydrogenase)
Thyreoid hormone diseases
SCID, X-linked
SCN4A (Kanalopathy; natrium)
Smith-Lemli-Opitz Syndrome
Spastic paraplegia, X-linked type 2
Spastic paraplegia, (SPG4), hereditary
Musculardystrophy, congenital (with merosinedeficiency)
Spinal muscular atrophy (SMA)
Spondyloepiphysary dysplasia tarda
Stickler Syndrome
Thyreoid peroxidase deficiency
Torsie Dystonia, early onset
Tuberous Sclerosis
Tyrosine hydroxylase deficiency (L-DOPA responsive dystonie)
Tyrosinemia type I
Unverricht-Lundborg disease (EPMI)
UPD
Vitamine E deficiency
Von Hippel-Lindau, disease of
Waardenburg Syndrome, type 1, 2 en 3
Wilson, disease of
Wiskott Aldrich Syndrome

Future developments

The increasing role of the private biotechnology sector is expected to influence the functioning of the centres, but the pace and impact of these developments is yet unclear, and stakeholders in the centres take different positions towards such developments.

Little interest in European harmonisation seems to exist, mostly because these centres function within the national health care system and cross-boundary linkages concerning patient materials

are limited. Similarly, a centralised facility to maintain collections appears irrelevant, given the primary role of the centres in health care and the patient-oriented sampling approach.
The issue of intellectual property rights obtained based on samples may raise problems in the future.

Representative collection data
In Leiden University Medical Centre, collection building started in 1982 through molecular analysis for Duchenne muscular dystrophy.
Currently 20,000 DNA samples are stored and a further increase rate of 10,000 samples per five years can be expected. The number of tissue samples amounts to 300 and is expected to grow to 600 over a five-yer period. The figures for cell lines are currently 1000 and a prognosis of 1500 within five years. Cell lines are mostly established for future use as certified reference materials. Most samples relate to families with genetic deficiencies, and approximately 300 pathologies are covered. Samples are obtained through the departments of the LUMC, and as a legal deposit in the case of forensic requests. Samples have now been storde up to 20 years and the average length of storage is expected to increase over time, since - except for the forensic materials - no samples are discarded.
The database has been built using Oracle software.
Sterlab accreditation has been obtained in 1998 and since then all samples are analysed and stored in duplicate. Standard Operating Procedures have been established, e.g. for storage conditions.
Presently, 100 genetic diseases are tested in Leiden.

The current size of the collections managed by the Centre at the Free University is estimated at 1000 cell samples and 5000 DNA samples approximately. The 5000 DNA samples relate to individual patients (4000) and families (1000) respectively.

Current size of the collections managed by the Erasmus University in Rotterdam are close to 25,000 cell samples and 25,000 DNA samples. At a yearly basis the centre in Rotterdam carries out 400 diagnoses of hereditary metabolic diseases, based on cell samples. In 1997 DNA diagnostics were performed on approximately 2600 individuals, These persons belonged to over 1500 families. The number of samples of dermal biopts or cultured fibroblasts received by the cell bank amounted approximately 400 in 1997, whereas the number of prenatal dianoses amounted to 1800.

The size of the DNA collection at the department by the University of Utrecht which only started work in 1995, is approx. 4000, including more than 500 families.

Raw questionnaire data

Plant domain

Table 6. Status, area, scope and size of the collection holder

Status of the institution	Nr of inst.
Part of network	2 (1)
Public	3 (1)
Non-for-profit	9
Research	7
Education / Teaching	2
Administration	2
National activity	5
National / International	2
International	2
Staff size Less than 10 From 10 to 49 From 50 to 249	 6 3 1

Table 7. Kind of samples maintained.

Kind of material	Nr. of answers
Plants in vivo	3
Seeds	5
Seeds & plants in vivo	1

Table 8. Duration of sample storage

Duration	Nr of answers
1 - 5 years	1
5-10 years	1
>10 years	7
blank	1

Table 9. Primary purpose of collections

Purpose	Nr of answers
Conservation of biodiversity	7
Utilization	5
Breeding	3
Technological application	1
Research	7
Legal requirement	1

Reference collection	5
Other purposes	1

Table 10. Type of documented data

Documentation	Nr of answers
Passport data	5
Evalution data	5
Pedigree/genetic relationship data	2
Molecular data	1
User data	5
Other information	1
blank	2

Table 11. Means of acquisition of materials

Acquisition by:	Nr of answers
Purchase	1
gift or exchange with other organisations	7
own efforts e.g. collecting missions	3
legal deposit requirements	3
Blank	1

Table 12. Information management

Method of information diffusion	Nr of answers
Publication	4
Catalogue	3
Electronic database	2
Internet site	3
Patent application	0
Other IPR	0
Other information diffusion	6
blank	2

Table 13. Kind of scientific activities carried out on the collections

Activity	% of total activities
Conservation	42
Characterization	21
Evaluation	8
Legal requirements	25
Promotion of utilization	9
Other purpose	10

Table 14. Collaboration

Collaborative activity	Nr of answers
Co-operation	4
EU programmes	1
breeding companies	2
public institutes	2
professional associations	2
NGOs	3
farmers	1
other organisations	2

Microbial domain

Table 15. Status, area, scope and size of the collection holder.

Status of the institution	Nr of inst.
Part of network	2
Public	4
Non-for-profit	7
Research	9
Health care	2
Education / Teaching	4
National activity	2
National / International	1
International	6
Staff size	
Less than 10	5
From 10 to 49	2
From 50 to 249	2

Table 16. Kind of samples maintained.

Kind of material	Nr. of answers
Microbial materials	1
Microbial Strains	5
Strains & serotypes	1
Strains+pathotypes	1
Virus strains	1

Table17. Duration of sample storage

Duration	Nr of answers
1 - 5 years	0
5-10 years	0
>10 years	9

Total	9

Table 18. Primary purpose of collections

Purpose	Nr of answers
Conservation of biodiversity	3
Utilization	6
Breeding	1
Technological application	4
Research	8
Legal requirement	2
Reference collection	6
Other purposes	1
Total	9

Table 19. Type of documented data

Documentation	Nr of answers
Passport data	0
Evalution data	2
Pedigree/genetic relationship data	1
Molecular data	4
User data	0
Other information	2
Not answered	3

Table 20. Means of acquisition of materials

Data	Nr of answers
Purchase	5
gift or exchange with other organisations	7
Acquisition by own efforts e.g. collecting missions	8
legal deposit requirements	3
other organisation of sample acquisition	2

Table 21. Information management

Method of information diffusion	Nr of answers
Publication	6
Catalogue	3
Electronic database	6
Internet site	3
Patent application	3
Other IPR	
Other information diffusion	1

Table 22. Kind of scientific activities carried out on the germplasm

Activity	% of total activities
Conservation	24
Characterization	28
Evaluation	13
Legal requirements	15
Promotion of utilization	25
Other purposes	25

Table 23. Collaboration

Collaborative activity	**Nr of answers**
Co-operation	7
EU programmes	3
Breeding companies	3
Biotechnology companies	5
Food a nutrition companies	4
Public institutes	7
Professional associations	2
NGOs	2
Farmers	1