Strategic Vision 2017-2021

European Huntington's Disease Network

Content

Introduction: Why a new strategic plan?

EHDN's strategic plan 2011-2015 laid out the foundations of the organization, its mission, aims and objectives and the strategy necessary to achieve all this. At that time EHDN had grown into a well-organized and consolidated European-based network that was able to design and conduct high-quality preclinical and clinical research studies. Moreover, it offered a network of clinical centres for HD patients that both served the direct interests of these patients and their families and were part of the infrastructure necessary to conduct clinical research.

In the past five years much has been achieved. Important clinical trials have been conducted that used the existing infrastructure and more are to follow. New countries with significant cohorts of HD-affected people have been included and local researchers in these countries have proven their mettle and commitment. Relations with CHDI, the primary sponsor of the EHDN network, are productive and fruitful while pharmaceutical companies are interested in what EHDN has to offer.

Yet, the period covered by the previous plan has ended. This has prompted EHDN's executive committee (EC) to review what has and has not been achieved, and what challenges and opportunities will arise within the next years. A new strategic vision is necessary – a plan that considers EHDN's status, structure and ambitions in the context of developments in the worldwide HD community. This plan should not only focus on scientific opportunities and challenges but should present a more comprehensive analysis of and statement on how EHDN should proceed in the years 2016-2021.

1. Evaluation of the previous plan and activities

Recapitulation: EHDN's mission statement 2011-2015

EHDN's mission as formulated in the previous strategic plan has been central to the organization's activities in the past years: to advance knowledge of Huntington's disease by supporting scientific and clinical efforts to develop and test therapeutic interventions that will improve the quality of life of people with Huntington's disease.

More specifically, ambitions include progress in the related areas of:

- Science: to advance scientific and clinical knowledge of Huntington's disease
- Treatment: to develop and test efficacious therapeutic interventions
- Care: to improve the health status of patients, at-risk individuals and family members of people with Huntington's disease

EHDN aims not only at taking care of tomorrow's patients by helping to discover and develop interventions for the future, but also to improve the lives of those affected by HD today, by setting

standards of care and helping to organize the best possible conditions for them to achieve good quality lives.

Strategic plan 2011-2015

EHDN's previous strategic plan that spanned the years 2011-2015 was very specific in what EHDN should set out to do. Its objectives and aims were formulated as follows:

1. Improve scientific governance
   a. Creation of a Scientific Planning Committee
   b. Creation of the Research Manager Position
   c. Reorganize EHDN staff support
2. Implement support facilities to improve scientific output
   a. Biostatistics support facility
   b. Clinical methodology support facility
   c. Medical writer support facility
   d. Designation of a study coordinator from the EHDN staff for every project
   e. Transitory plan to conclude ongoing studies
   f. EHDN scientific fellowship
3. Improve EHDN's capability to design good-quality clinical trials
   a. Creation of a Clinical Trials Task-Force
4. Improve EHDN's capability to conduct clinical trials
   a. Implement mechanisms to conduct all scientifically relevant analysis from REGISTRY and other EHDN-related studies, thus increasing knowledge on how to design clinical trials
   b. Support the development, validation and qualification of progression markers
5. Refocus the objectives of all active groups (mainly WGs) in accordance with EHDN´s main mission
6. Optimize research funding
7. Stimulate scientific collaboration
8. Improve training (scientific and clinical)
9. Improve communication (between the EHDN groups and with the HD community) and EHDN's public recognition
10. Develop an innovation area
11. Guarantee sustainability
12. Monitor the plan implementation
13. Review the plan

These objectives formulate scientific ambitions, as well as EHDN's structural and organizational requirements necessary to fulfill these ambitions. The aim of finding novel and evaluating existing treatments is explicitly addressed, but the issue of how to improve health status and care for affected individuals and their families, mentioned in the mission statement, was not visible in the 2011 objectives.

How successful has EHDN been in stimulating and initiating groundbreaking research? Establishing and expanding the huge Registry database has been the network's major success. It formed the basis of many subsequent endeavors. It should be pointed out that this database wouldn't have been achieved without the help of our North American partner CHDI.

Improving EHDN's capability to design and conduct clinical trials (objectives 3 and 4)

This has been a major effort over the past years. The network's strong infrastructure has led to it being a major player worldwide in terms of capabilities to conduct clinical trials (objective 4). Many EHDN sites have contributed to trials while individual EHDN members have been very active in their design and initiation (e.g. DBS, TRACK-HD, biomarkers). Also, members have contributed substantially to trial methodology for HD patients. TRACK-HD would not have existed without EHDN and its biomarkers working group. Also, the establishment of a Clinical Trials Task Force (CTTF; objective 3) has led to a more systematic approach towards the acquisition, introduction and conduct of trials. Quality improvement has been a major issue for CTTF and this effort is still ongoing. Due to expanding requirements for compliance with regulatory standards, over the next years EHDN will have to devote increasing amounts of resources to the operations of this task force.

Did this make EHDN a partner to industrial parties? Potential commercial partners primarily liaise with CHDI or with individual research groups, not with EHDN. Yet, EHDN's Clinical Trials Task Force has succeeded in attracting various company partners, bringing them in contact with individual research groups, while operational support provided has contributed to successful trial execution. Thus, part of the success of the recognition of the network as the creator of an environment that allows the conduct of high-quality trials has been the work of the CTTF. Progress monitoring, site certification and liaison with industrial partners did contribute to this recognition. In this, CTTF has been quite effective.

Thus, EHDN has significantly and relevantly contributed to initiation, design and development of trials and without EHDN the field would not have advanced as well as it has. But the network has not been an organization that conducts trials itself; it is primarily an organization that facilitates the conduct of trials in individual clinics. As an organization, we perceive no compelling reason to change this in upcoming years

Improving scientific governance (objective 1)

A solid organizational structure that unifies, inspires and facilitates HD related work in Europe has been achieved. The strong central infrastructure in Ulm is the organizational and administrative core of EHDN's international activities, both in terms of research endeavors and network organizational activities.

The Scientific Planning Committee (SPC) did not work out as anticipated. Intended as a committee to initiate and guide research in a top-down manner, the number of projects that emanated from it has been very limited. It should be acknowledged that SPC has been successful in harmonizing Registry with its successor Enroll, but this harmonization task is now finished.

The reasons for SPC not reaching its intended potential have not been formally analyzed, but apparently its tasks and responsibilities were insufficiently defined. Moreover, the fundamental question whether EHDN should top-down initiate research may be part of the answer.

In contrast, the existence of EHDN almost certainly has played a role in the initiation of basic research and in interesting young researchers for HD research. Several working groups have been instrumental in generating novel ideas and identifying research needs (see below), while the availability of seed funds has almost certainly drawn additional researchers into the field. This holds true for both basic and applied / clinical research. Apparently, EHDN's current structure has stimulated a bottom-up process.

Implementation of scientific support facilities (objective 2)

To maximize scientific output of EHDN's associated research centers and single investigators, a number of support facilities were proposed in the previous plan: biostatistics support, clinical methodology and medical writing. However, although such support was made available to HD researchers, very few applications have been received. A few requests for reviewing manuscripts by a medical writer have been awarded, but apparently there was no major need for this centralized service. Most researchers used their own institutional facilities. Central Coordination / EHDN staff on projects/trials provided necessary expertise and CHDI has a statistical committee that can support researchers.

A Grant and Collaborations manager was attracted, with the intention that he/she would help acquiring major multinational (particularly European) grants.[1] A few applications have used the services of this grant manager (ERN-RND, H2020 consortia / Visegrad, Gossweiler) but the overall yield of major European subsidies for HD-related research has been low. Reasons became apparent over the past period. HD and EHDN visibility within the European political environment are limited. Individual researchers and research consortia seek grant application support primarily from their own institutional services, and EHDN is not a legal entity and thus not a partner in applications.

Based on this, the tasks of a grant manager, and more broadly, of Central Coordination, may have to be redefined. Activities may include: screening and identification of potential grant opportunities; tailored advice to specific researchers and responding to individual queries about grant opportunities; following the policy landscape and developments in Europe and internationally regarding rare diseases / movement disorders / neurodegeneration; strategic advice and support regarding positioning of EHDN within a European framework (specifically: European Reference Networks); networking and advocacy for EHDN; promoting and forming links with all relevant stakeholder groups; promoting visibility, outreach activities and information exchange with potential stakeholders at all levels (including social media activities).

[1] Activities and achievements have been described in a separate document: Grant and Collaborations Manager (G&C Manager)– lessons tailoring future activities.

Refocusing the objectives of working groups (objective 5)

From EHDN's inception onwards, working groups have been part of the network's structure. One of their primary aims was to enable those who were part of the Registry study teams to feel invested in the study – to give a sense of ownership and responsibility. EHDN participants should not solely be instrumental in collecting data but also be able to generate scientific ideas, help developing the database, use database content and come up with suggestions and guidelines as to how to improve disease management and care of people with HD. Several groups have been highly successful. The Quality of Life, Genetic Testing and Counseling and Physiotherapy Working Groups have all produced international guidelines. The Biomarkers Working Group gave rise to TRACK-HD that in turn gave rise to TRACK-On. This helped defining detailed HD phenotypes that can be used in clinical trials. The Genetic Modifiers Working Group contributes to the Genetic Modifiers of HD study consortium and was instrumental in getting changes in data collection incorporated into Registry, and subsequently in Enroll-HD, to enable advanced genetic analysis, the high quality video material generated by the motor working group, which has been the basis of training for more than 10 years.

But not all working groups have been similarly successful, some having led languishing or dormant existences. A recent review identified factors that contribute to a successful working group. Committed leadership with drive and perseverance, clearly focused questions or tasks, achievable objectives, and appropriate input from EHDN greatly contribute to success. Negative factors are lack of collaboration between WGs; lack of leadership; stagnant membership; no specific plans, objectives or tasks; lack of updating of active membership; and lack of up to date information on the website. Also while WG meetings are financially supported by EHDN, the contribution of members is purely voluntary, making independent WG contributions for specific projects between meetings difficult to prioritize during working hours.

Optimization of research funding; seed funds (objective 6)

EHDN's network activities have been made possible through the generous support from CHDI. It is arguable whether support for its organizational activities should be sought from others outside CHDI - as dependency on one funder makes the network highly dependable upon future developments of that funder..

The actual aim of this previous objective was to stimulate interdisciplinary collaborative research, primarily in Working Groups, not only through seed funds (that come from CHDI), but also through novel revenue streams. As concluded in the previous paragraphs, attempts to obtain such 'outside' money / external grants were initiated by ad hoc consortia of researchers that might or might not collaborate in the various Working Groups. As such, neither EHDN nor its Working Groups are independent legal entities, a requirement for receiving grants. However, they provide the forums in which individual members might build ad hoc grant attracting collaborations.

Already prior to the formulation of the previous strategic plan, seed funds were available to help researchers obtaining larger grants. All previous seed fund recipients have been contacted, to evaluate whether they have been able to publish their work, generate new data and get additional funding. Of

the 52 projects granted, two were never claimed (one recipient was on a long sick leave). By the end of 2015, of 43 ongoing/accomplished projects contacted, 35 recipients returned questionnaires; 23 projects were finished. The number of seed fund related project published papers was 25, of which 5 are in JHD or PLoS Curr HD, with more in preparation or under review. Over the years the number of seed fund applications has steadily risen. A limited number of projects has yielded successful large grant applications, the most notable being the German Deep Brain Stimulation study.

Improve communication (between the EHDN groups and with the HD community) and EHDN's public recognition (objective 9)

Within EHDN the regular meetings and the joint interests have established good working relations between the various network members. However, outside the field EHDN needs to be known better. Neither policy makers nor other rare neurodegenerative disease consortia appear to have a clear view of what the network represents.

EHDN as a science organization?

Although not stated explicitly in the previous plan, many within EHDN have considered the network to be able to play a central role in worldwide HD research. This implies a top-down policy and a structure that stimulates and facilitates a number of process steps. In such a vision issues to address would be:

- Who formulates relevant scientific questions and ideas? (Working groups and the Scientific Planning Committee should play a role in this, as do the lay organizations.)
- How to work with Patient Associations? How to formalize input regarding research priorities? (Close involvement of EHA)
- Who is stimulating collaboration between research groups inside and outside Europe? (Working groups; meetings.)
- Who is identifying larger infrastructural needs?
- Who is helping to obtain major grants for these larger needs? (A Grant and Collaborations manager.)
- How do we communicate at various levels, particularly with people and organizations outside EHDN? (A communications strategy.)
- How do we disseminate results to the outside world? (Conference presentations, publications. A communication strategy.)
- How to organize interaction between clinicians and basic researchers? (Meetings.)
- How to organize creativity and project proposals bottom up? (Working groups.)

Clearly, a number of these structural and process requirements have been implemented over the past years, and even more effort should be put into this.

An important factor is EHDN's legal status – which it does not have. The network's facilities, e.g. Central Coordination, are part of Ulm University.

If EHDN would consider itself as a science organization, a critical evaluation of success should consider the quantity and quality of research papers published by its members. Efforts already in place have the potential to be further developed. .

Other activities (objectives 6 to 11)

EHDN has been highly successful in stimulating scientific collaborations, both within and between its working groups, as well as with people in the broader international research community. Examples are the consortia that were formed in a very short time to prepare projects for H2020 submissions. At EHDN's biennial meetings the HD community from all over Europe, indeed from all over the world meets in a highly collaborative and stimulating environment. Thus, the network provides one of the strongest forums on HD research in the world. The HD fellowships have improved training, both scientific and clinical, for young researchers and clinicians. Moreover, the liaison with EHA and national lay organizations demonstrates its fullest implementation at these meetings.

What has insufficiently been achieved from these meetings is communication with the world outside the HD community. Press attention and participation from other groups, for example representatives from other rare disease communities, is still limited, although efforts have been initiated. A policy speaker from the European Commission made a presentation at the recent Plenary meeting in The Hague. Clearly, such opportunities should be followed up in a systematic way. Representatives from other rare disease networks should be invited and more extensive press coverage should be sought in advance.

The status of care activities

Has EHDN been sufficiently instrumental in improving care for patients with HD? Care has explicitly been mentioned in EHDN's mission. It should be pointed out that under the aegis of the network and inspired by it, HD clinics have been established in a number of European countries that did not yet possess such expertise. Standards of care have been formulated by various Working Groups and international guidelines have been produced and implemented in a number of European countries.

A training program was established that offered young starting clinicians the opportunity to acquire detailed knowledge of the disease and its complications. Dedicated working groups are still active that tackle issues of care. Thus, improvement of care for patients and their families has been realized as a result of EHDN members' efforts over the past years and the results have been recognized by lay organizations and families, as well as others.

An opportunity to further improve these care related activities may be offered by broader collaborations with other 'rare diseases' networks, e.g. ERN-RND network.

Current Strengths, Weaknesses, Opportunities, Threats

Part of the evaluation process of the previous Strategic Plan was a discussion within EHDN's executive committee on the strengths, weaknesses of EHDN and the external opportunities and threats that face the organization. The opinions and insights from this discussion provide the basis for the new plan.

Strengths

Clear ***organizational strengths*** were recognized. EHDN is currently a strong and reliably funded organization with professional and competent members, staff and collaborators who maintain the defining network activities. The organization has an explicit mission statement that has been defined in the constitution. Its current focus is to encourage and sustain HD research. For this, a functional structure based on the strategic objectives and a recognizable governance have been implemented. EHDN's major asset – and indeed a major reason for its existence - is the trial infrastructure that facilitates a crucial and recognized role in trial protocol endorsement and clinical trial execution.

Another major strength are the strong ties to ***patient and lay organizations***, particularly EHA. Representatives of EHA participate in EHDN operations and functioning at the highest level. The participation of engaged patients, family members and caregivers has been unwaveringly strong and supportive. Apparently EHDN has been able to retain their interest and involvement.

It's ***people*** who make an organization. EHDN has been able to involve not only those who are most directly affected by HD every day, but also almost every clinician and researcher in Europe who has devoted her or his professional life to the disease. EHDN's broad and competent membership and the resulting collaborative network of patients, family members, caregivers, clinicians and researchers has proven its mettle. A large number of clinical sites has sprung up that allow efficient conduct of clinical trials.

The working groups embody the bottom up activities. And the overall quality, professionalism and enthusiasm of all those involved is supported by the activities of the language coordinators, the Lancos. EHDN stimulates and motivates.

Weaknesses

A number of weaknesses were mentioned in the discussions.

Some are related to EHDN's current ***mission and identity***. Some members fear that EHDN may suffer from a lack of focus, as exemplified in the previous mission statement. We may attempt to accomplish too much in different areas – basic and clinical research, care, training, expansion over Europe. It is currently not clear to everybody which direction the organization should take. Different participants may have different ideas.

Part of this lack of direction may have to do with a temporary lack or a loss of identity after the transformation of Registry into Enroll. The combination of a European perspective and a joint – but also somewhat exclusive – participation in Registry did infuse enthusiasm in the collaboration. Now that all European groups and participants are part of a worldwide endeavor that is basically run from the United States, the question arises what EHDN as a separate organization stands for. Clear aims that transcend the initial collection of clinical data are needed. Clinical interventions aimed at symptomatic relief may be an example of such motivators.

Although the collaborative spirit between the various European researchers that participate in EHDN has always been high, actual research projects and programs are being run by independent *ad hoc* consortia tied to EHDN but not part of EHDN's formal structure. In this respect, the network is a platform for people to meet - an important platform but not a research organization.

From the clinical perspective, international guidelines for care and treatment have been formulated but EHDN has not been instrumental in the actual national implementation of guidelines. Again, the platform is able to bring people together but it is not a clinical support organization.

Lack of identity may have to do with ***branding***. Communication with the outside world about what EHDN is and offers is presents a major opportunity. Until now, the network has not developed a general communication strategy and perhaps never even considered it in a formal process. One indicator: the website is outdated.

As a result, actual or potential partners have little awareness of the network. For individual researchers, being part of EHDN apparently holds no sway over potential international research funding programs such as Horizon 2020 or JPND. From a clinical perspective the lack of a communication strategy becomes apparent in a lack of international educational activities directed towards those outside the EHDN membership. There is no promotion/lobby strategy for using unified European-wide processes at the European Medicine's Agency, EMA. Communication with other rare disease networks is still in its infancy and not part of an overall coherent strategy. And even though the ties to the lay community are strong, structured interaction at national or local levels can improve. Are the local chapters of the various national lay organizations sufficiently integrated and aware of the benefits that EHDN may bring? Is the network visible and accessible enough for them?

EHDN's ***organization*** is strong in many respects, but some weaknesses can be identified. The network's legal status is unclear. It is not a legal entity by itself but dependent on Ulm University as its representative. Not all European countries are incorporated in EHDN. It is unclear whether the implementation of the central top down strategy as formulated in the Strategic Plan 2011-2015 has been successful. Differences and imbalances between regions exist, perhaps caused or aggravated by the complexity of the network and by difficulties in handling the multinational / multi-language context within Enroll-HD. Or is this simply due to the geopolitical and socioeconomic circumstances unrelated to HD? Heterogeneity between functional units exists and collaborations across Working Groups are of variable strength and intensity. And, very important: a lack of young leadership may threaten the network. There is currently no program to address this deficiency.

At the ***operations*** level there is still room for improvement. Efficiency and effectiveness of the network's operational efforts is variable, related to variable levels of professional involvement and commitment of the network members. Network procedures have always primarily been geared towards one dominant effort: Registry and its successor Enroll. How successful can other challenges be dealt with? As an example: specialty-training for HD clinical care is lacking, although the fellowship program is a first step to address this lack. Enroll (and previously Registry) requires that every participating clinical researcher

adheres to a minimum level of knowledge and clinical skills. Similar requirements do not exist for clinical care.

As part of internal operations, procedures and criteria for systematically evaluating scientific quality of network efforts is lacking. We do not have criteria to judge the performance of the network as a whole.

The final area where weaknesses can be defined is ***funding***. EHDN is totally dependent for funding upon one single sponsor; others have never been attracted – they were not necessary. The generous single sponsor funding is comfortable for the network but it carries the twin risks of vital dependency and complacency. If the sponsor stops, EHDN is probably no longer viable. Also, it should be noted that EHDN's elected EC leadership has no budget responsibility and does not discuss budget allocations. The situation is compounded by - or perhaps even causative of – the fact that the success rate of major European grant applications (H2020, JPND) for HD-related research has been low.

Opportunities

There are clear opportunities identifiable within the ***social and political context***. Interest in Europe in rare / orphan diseases is growing, as it does elsewhere, and HD is one of the better known orphan diseases. This interest originates not only from decision makers in the various European countries, but also from the European Union itself, as well as from a broader lay public. The perspective of these parties is not exclusively on science but also on care delivery, organization and professional training. European funding programs for training, health care quality and service improvement are available.

EHDN should be optimally positioned to benefit from this rising interest. Although it may have to compete for attention with other rare diseases, the strong links with the lay organizations and other stakeholders, the obvious spirit of European collaboration, and the absence of a competing European HD organization provide a strong base. Opportunities for expanding into other countries still exist and such expansion will only strengthen EHDN's position. EHDN should be the ambassador for people and families with HD in Europe in conjunction with the HD patient advocacy groups.

An active policy of collaboration with other rare neurodegenerative disease consortia and organizations may aid in this social and political context. Such collaboration may provide leverage in the struggle for priority, attention and funding in Europe.

This is not only relevant to EHDN but also to EHA, the network's strongest ally and actually closely intertwined with EHDN. The ***growth and strengthening of EHA*** provides additional strength for EHDN and vice versa, in an environment that increasingly values health research and health care as predominant interests of those affected: the patients, the families and their caregivers. More input of EHA in setting research priorities and focus of EHDN certainly will benefit the network.

Another opportunity is the acquisition of ***additional financial support***. Network funding is available from a number of national and European grant agencies. The network has never examined the priorities and preferences of potentially relevant philanthropies.

From a ***pharmacotherapeutical research perspective***, HD may have some unique 'selling points'. As a pure monogenetic disorder with a single 'quantitative' mutation, it is considered by many as a model disorder, particularly a model for dementia. Funding for dementia research is abundant which has raised the interest of a number of pharmaceutical companies. These companies currently have pipelines for novel disease modifying compounds or are testing novel applications for existing compounds.

The way HD is studied by the EHDN community (as well as the international HD research community) is cutting edge. There is major interest for the existing Enroll (former Registry) database and the wealth of clinical data it contains. The structure of the data entering and collection platform, the size and structure of its data set and the potential for testing and applying novel analysis technologies provide ample opportunities for clinical research in the era of big data research.

Weaknesses identified in previous paragraphs are related to the relative invisibility of the EHDN and its endeavors. ***Rebranding*** the network through an active communication policy may facilitate the fulfillment of opportunities mentioned.

Threats

The threats that face the network are obvious. In the current situation, the loss of EHDN's ties with its sponsor CHDI will effectively terminate the network. A more gradual decline will set in if EHDN becomes less relevant, e.g. in a scenario in which Enroll becomes truly global while recruiting rates in Europe decline. Also, competition from other organizations for projects and funding may diminish the network's role.

Another risk of decline is related to the inherent difficulties of the task the network has set out to achieve. Neurodegenerative diseases are intrinsically difficult to treat and a sustained frustration caused by not seeing results may demoralize patients, researchers and particularly the pharmaceutical companies that have entered the HD field. HD is a rare disease, the road to truly disease modifying therapies is long and expensive, and other, better reachable targets than 'cure' may not be attractive to companies. Once true prevention trials start, the actual number of potential participants that can be enrolled may become a limiting factor in conducting such trials. Regulatory issues such as privacy and intellectual property may become so complicated that HD trials become no longer feasible from the economical perspective. Moreover, a tendency towards deglobalization that is currently visible, both in Europe and in the United States, may create a fragmented regulatory environment, which increases costs for pharmaceutical companies to develop truly novel medications. In case of initial high pricing of effective treatments, national reimbursement issues will appear.

Again, the general perception of what HD is and what the network stands for should always be guarded. Negative stories, loss of patient commitment, loss of sponsors' commitment and a lack of interest from the public because 'there is no risk outside certain families' may be detrimental.

2. Strategic plan 2016-2021

What is EHDN's identity?

EHDN's identity is linked to its fundamental purpose described in EHDN's mission statement. This mission statement normally remains unchanged over time. It (1) serves as a filter to distinguish what is important from what is not, (2) clearly states who our beneficiaries are and how they can be served, and (3) communicates a sense of intended direction to the entire network.

Who are we?

EHDN is a network of European researchers, clinicians and other health professionals as well as people affected by HD. The network is dedicated to understanding Huntington's disease and facilitate the development of treatments and other related support for those affected by the condition. Network members are committed to research, finding novel and evaluating existing treatments, and to providing guidance as to how care for people affected by HD should be organized.

What do we do?

EHDN provides a human resource infrastructure, a forum for researchers, clinicians and those affected by the disease to meet and work on HD. The organization strives to achieve better understanding of and care for people with HD in Europe. EHDN attempts to decrease barriers to get things done.

This is how we see ourselves. How do others see us? What do the lay organizations and the individual patients and their families expect from us? How about CHDI, our major international partner? How should we define our relation towards representatives of other rare diseases? Do we have an identity to present to health policy makers and colleagues in other fields?

We are not an organization that competes with other European organizations for funding or projects. EHDN's separate members as well as organizations outside the network will run the scientific and clinical projects. EHDN's task is to support and facilitate these projects as much as possible.

Why do we need a European network, why not collaborate in a more global context – which is already what Enroll provides? EHDN's current structure, its history, the convergent national health care systems, the opportunities for European grants, and the cultural identities and values that members share with each other and with people in their respective countries who are affected by HD, all argue in favor of a joint European endeavor. A global outlook and global collaborations are part of our professional lives, but we do value a distinct European network.

Restatement of Mission

It is EHDN's mission to improve the lives of people affected by HD.

Objectives and Strategies

The network wants to:

- Advance research
- Conduct trials
- Improve care

All this should be accomplished by EHDN's individual collaborating members, by the sites and centers that constitute the network, by the staff that supports and sustains the network activities, and by collaborations with external groups and organizations such as companies and other rare diseases networks.

Future directions/strategies: Advancing Research

It is part of EHDN's objectives to facilitate research, both clinical and more basic research. The network itself does not perform research projects; neither does it conduct or develop 'top down' research programs. Instead, it offers help, access to people affected by HD and support to those embarking on specific projects.

Over the years, EHDN's fundamental scientific, systematic and continuous activity has been systematically collecting clinical data and facilitating clinical trials. Obviously, this will remain the major activity of the network in the upcoming years.

But the challenge to the network is also to continue to encourage the formulation of novel questions and the initiation of new projects. Research endeavors can be proposed and initiated by individual members, by working groups, by CHDI, and by other companies. These parties are eligible to request support from EHDN. A process of evaluation by the network should precede actual endorsement and support. In addition, evaluation of completed trials and projects should be part of the network's operations.

To help implementing these three functions – encouraging novel questions and projects, endorsing specific proposals and evaluating completed projects and trials - a new Scientific Coordination Committee (SCC; see below) should be established Also, parts of this work should be delegated to SBAC.

Working Groups

In the upcoming years working groups will remain important components of the network. They are essential for the bottom-up process of generating novel ideas and projects. But given the insights mentioned in previous paragraphs, working groups should be more stringently managed. Those that are no longer active should be identified and be formally discontinued. Those that are active should be provided with clearer general directions.

Working groups are expected to:

- support EHDN strategy;
- support work to improve the lives of people with HD and their families;

- support work necessary or useful for clinical trials;
- tie into scientific strategy and clinical trial committees;
- be active - give rise to "task and finish groups" that carry out projects to achieve specific goals, make specific decisions or weigh evidence, lobby;
- engage HD researchers and those outside HD who have relevant expertise;
- engage HD patients, families and the at risk population as appropriate;
- open the participation to selected specialists outside of Europe

In addition, Working Groups should:

- work together to complete specific and defined objectives that align with the EHDN mission;
- aim to answer questions from the scientific strategy or clinical trial groups of Enroll;
- be prepared to to lobby health care providers to best fulfill the needs of HD patients and families;
- aim to respond to specific grant calls or to anticipate/lobby around grant calls.

Tasks for the EC in this respect will be:

- to motivate active working groups and to follow them closely, e.g. by inviting them to regular meetings;
- to help to support new and relevant projects that come from active working groups;
- to help disseminate on-going discussions, activities and projects in specific working groups, e.g. on the website or on social media;
- to identify those working groups that are no longer active and to remove them from the website.

Developing better communications with active working groups may help to develop their ideas into actual projects. Current pilots that emerged from the working groups have requested seed funding, some have led to quite large observational studies but these projects have hardly ever been followed up by large-scale trials. The SCC may monitor their activities while Central Coordination may actually help develop projects into viable grant applications.

Patient driven and care driven research questions should be actively sought through closer collaborations with the patient associations, particularly EHA. The newly formed CTAC (Clinical Trial Advisory Council), a patients and families initiative that involves associations in Europe, the UK, USA and Canada, should be actively consulted on upcoming trials and care projects. Already, many funding agencies require patient involvement to be explicitly covered in individual applications. Here, EHDN researchers have unique opportunities given EHA's role and involvement in the network.

Collaborations with other 'rare diseases' networks potentially provide ample opportunities, both in terms of interesting science and novel insights, and in terms of visibility and political clout. Participation in the ERN is a first step in this direction.

Future directions/strategies: Conducting Trials

Providing opportunities for clinical trials is clearly one of the aims and strengths of the network. In this respect EHDN offers its services to the international scientific, clinical and business community. The strategic challenge is not to formulate the type of trials that should be performed in the next years, but to formulate the conditions that are optimal for conceiving and executing clinical trials. What are these conditions?

Current trials are often initiated and driven by interested companies. Such collaborations are valuable and in fact one of the reasons for EHDN's existence. To make EHDN members and sites attractive to trial sponsors, an active policy of GCP site training and certification should be pursued, in close collaboration with our North American colleagues in HSG, as ethical and regulatory requirements are fundamentally global.

How may companies that explore novel therapeutics are attracted to the network and to its members - clinics and individual researchers? Clearly CHDI has helped a lot, but the network itself should create worldwide awareness by being a visibly strong organization and maintaining an active communication plan.

Future directions/strategies: Improving Care

In considering future activities regarding patient care, the first question should be: what does EHA expect from EHDN? The consequence of this is organizing systematic discussions with EHA.

Further development of guidelines and standards of care is necessary. Development of a portfolio of required guidelines, based upon 'real life experiences' and unmet needs should help structure these endeavors.

In terms of already available treatments: EHDN should continue taking initiatives on formulating treatment guidelines, as it has done in the previous years through a number of active working groups. Existing practices and unmet needs should be identified in dialogue with EHA and the national lay organizations. Relevant guidelines should be based upon the latest scientific evidence. Additional research should be proposed where obvious deficiencies exist in existing knowledge to support recommendations.

Training of young clinicians in the current Fellowship Exchange Programme should be continued. The program can perhaps be expanded by attracting additional funding, e.g. from the Movement Disorders Society (as has been achieved in 2017). Thus, more young clinicians will be exposed to HD care, with additional centers hopefully to be engaged that can recruit research participants.

Also, creating awareness of HD among clinicians from other specialties may be relevant, e.g. among psychiatrists, psychologists and rehabilitation specialists. Their involvement in HD care will add valuable insights and expertise, benefiting those affected by the disease.

Adequate patient care also involves political lobbying for the interests of those affected by the disease, both in the member countries and at the European level. Again, an active public relations (PR) policy is instrumental for this ambition.

Future directions: Structure of the Network

EHDN's current structure has brought the network where it is today. Components like Central Coordination and the Lancos have proven to be fundamental to the network's functioning over the past years. What additional tasks and responsibilities will EHDN assume and how will this change the network's structure?

One issue that has been discussed is EHDN's legal status in terms of its relation with CHDI. Legally, EHDN is part of the University of Ulm. CHDI funding is transferred to this institution and managed by EHDN staff and the University. Over the past years this arrangement has worked well and there is no need to change it.

EHDN's major effort has shifted from Registry to Enroll – from a European effort to a global effort. EHDN's staff and structures have seamlessly adjusted to the transition. In fact, EHDN staff plays a major part in the organization and execution of Enroll in Europe and globally. Obviously, the current staff and the organization are flexible, and up to the task.

Should EHDN's membership and its active sites be extended to additional European countries, or perhaps even adjoining areas like North Africa and the Middle East (Israel)? EHDN has always strived to be inclusive and new members will not be refused. But given the current magnitude of activities, there is no need to pursue active recruitment of sites and clinics in additional countries.

Scientific support from Central Coordination

Statistics support has been available at Central Coordination, initially and primarily for the purposes of Registry. The number of requests for the service from researchers has been negligible. EHDN is a network, not a research organization. . Recently an independent statistics committee has been organized by CHDI that serves the entire (international) HD community, primarily for planning trials. Therefore, such a central service embedded in EHDN is no longer necessary.

Scientific Coordination Committee

Ample opportunities exist for EHDN to provide guidance for HD research in Europe, as most HD researchers in clinical, translational and basic research are involved in the network.

The task of a newly established provisionally called *Scientific Coordination Committee* (the previous Scientific Planning Committee) is to explore and formulate unmet needs in HD research in Europe. This is based upon a thorough knowledge of the field, strong interactions with EHDN working groups, with CHDI, and with other HD networks, specifically HSG, and the Latin American and Chinese networks.

From this interaction project ideas should be formulated and discussed with the partners. Specific emphasis should be on EHDN's network experience, to make the best use of the platform. The new SCC should also strongly interact with the working groups, both to encourage and frame their activities as well as to receive input for their work. A high level of awareness about European grant opportunities (aided by the G&C manager) should help to match recognized needs with funding for collaborative projects. Also, the committee will ideally be the first party for companies to turn to when opportunities for trials arise.

The SCC itself will not directly be involved in actual research projects, grant writing and scientific communication. It will act as a think tank to support such activities run by individual EHDN investigators and consortia. This will prioritize initiatives from EHDN members for which collaboration with others is required. The SCC should also liaise with CHDI and other sponsors (primarily commercial enterprises) to judge feasibility of proposed research projects (including trials in collaboration with the CTTF and CHDI Outreach) for the network, to prioritize proposals and to help implementing projects that have been accepted.

A senior researcher, not belonging to operational staff, with a good knowledge of EHDN and other networks, should chair the SCC. Members should include three other senior HD researchers with each a clinical, a translational and a basic background respectively, at least one being a member of the EC and all appointed by EC. The SCC may collaborate closely with SBAC, asking SBAC to help evaluating specific research proposals and activities.

EHDN staff will support the SCC. This support will include the working group coordinator and the grant manager. Preferably, SCC should meet once a year in person and have bi-monthly telephone conferences with supporting staff. SCC should report to the EC on a regular basis.

Clinical Trial Task Force (CTTF)

CTTF is not an EHDN committee in a strict sense, the intention having been to bring together representatives from EHDN, HSG and CHDI. CTTF has proven to be an effective and useful contributor to network operations. Clinical trial support services i.e. trial monitoring, country and site selection and certification, and liaising with CHDI and interested drug companies have been important activities that have provided credibility to the network's operations. CTTF has been the major force that has improved EHDN's visibility with international pharmaceutical companies.

Thus, CTTF should continue to operate for the next years. Efforts should be made to bring in more HSG representatives. Also, one EHDN-EC member in the committee should streamline liaison and early awareness of upcoming clinical trials.

Scientific Bioethics and Advisory Committee (SBAC)

The SBAC is required by EHDN's constitution. Over the years it has developed efficient operating procedures. Its work on requests for Registry data mining will decrease in the next years but it will remain active reviewing seed fund proposals and new trial proposals, in parallel with and independently of the CTTF. Expertise on ethical aspects of proposals has been strengthened.

Important future directions envisioned are an increased emphasis on ethics considerations and feedback from patient associations. Also, proposal endorsement and evaluation of finalized trials and projects may constitute a novel task for SBAC, in line with what has previously been mentioned under 'Future directions: Science', closely collaborating with the new SCC..

The existence of an independent scientific and ethical review board remains crucial for the network's ambitions to be instrumental in conducting trials as well as more fundamental research.

Lancos

Language coordinators are indispensable for operations and activities of the network. They constitute the layer between EC and Central Coordination on the one hand and the various participating clinicians and researchers on the other, thus allowing for effective and efficient communications. Lancos are highly motivated, flexible and excellent advocates for EHDN's work. They not just support ENROLL HD activities but are involved in other projects as well. If a more pro-active overall communications strategy will be pursued, Lancos will be appropriate persons to implement both internal and external (national) initiatives, e.g. alerting national media to developments in HD research and care.

Rejuvenation of leadership

Like any organization, EHDN needs a policy to bring new and, ideally, young people into leadership positions, thus guaranteeing future strength and growth. Not only age but also nationality should be a consideration. The membership of the various committees (including EC) and working groups should reflect EHDN's multinational membership. It is EC's task to formulate a policy to this end and take appropriate initiatives.

Future directions: Visibility and Dissemination – Communication plan

One of the major issues identified in our SWOT analysis is the lack of visibility to the outside world. Although the lay organizations and most researchers in Europe are aware of EHDN's contributions, few people and organizations outside the HD community know EHDN.

In the next years the network will have to focus on visibility and bring the EHDN message to external audiences. For this, the Executive Committee will have to develop a central communication strategy. Central to a successful communication plan is a clear mission. This also fosters corporate identity and helps to maintain the spirit and enthusiasm of its members that is crucial to EHDN's existence and success. This has never been a problem; our aim is to maintain this spirit.

EHDN membership is currently Enroll's biggest contributor in terms of numbers of patients and family members participating and number of centers involved. For this to continue, it is important for the network members to share an identity that transcends the role of merely collecting clinical data. Important means to maintain enthusiasm are: continuation of regular plenary meetings; close collaboration with EHA as well as national patient organizations; identifying and facilitating successful

working groups; collaborations in research and clinical care projects; a visible national and European communications strategy that reaches out to external parties in the various countries; and maintaining a European identity.

The overall communication strategy is yet to be devised. However, it may contain the following:

- Telling the story of EHDN at congresses and meetings, in lectures, abstracts and posters.
- Approaching national media through press releases about major activities such as congresses, achievements, papers. Telling the story of HD.
- Creating public funding initiatives (like the ice bucket challenge in ALS).
- Presenting guidelines of HD care to national medical and nursing associations. Liaising with national quality of care organizations.
- Organizing training courses such as summer schools for health professionals and students.
- Lobbying at the EU level; trying to provide early input to research funding policies.
- Developing a pipeline of projects for funding applications that can quickly be adapted to the novel funding calls.
- A renovated website.

As a first step, EC should formulate a PR plan.

Future directions: Financial considerations

Currently, and in the foreseeable future, CHDI remains EHDN's only sponsor for organizational infrastructure and for seed funds. Being a network organization, it will be difficult to find additional sponsors, and in fact, such additional sponsorship is not necessary. Also, the network not being a research organization, has itself no need to attract additional funding that can be diverted into targeted research projects or programs.

Network members and collaborations based in the network will apply for research funding from other granting organizations. The network may support them in these activities. The investment in grant managing activities that was implemented in accordance with the previous plan unfortunately yielded disappointingly low returns. Targeting other activities, e.g. dissemination and visibility of network activity, may be more appropriate.

Collaborating with other rare diseases networks – e.g. the European Reference Network project – may be a better strategy to help members obtain research funding. But again, this would be primarily aimed at grant acquisition support for specific research activities of members, not to attract infrastructure funding for network operations.

One exception to this would be to attract funding for the various national lay organizations, as well as for EHA. In negotiating trial reimbursements with drug companies, funds could perhaps be allocated for specific activities for the various lay organizations. Their role in representing the interests of those affected by HD is important and relevant to every party involved in HD drug research.

Future directions: Monitoring of EC initiatives

In terms of how the EC operates, a restructuring of activities is necessary. The long term initiatives that are announced in this updated Strategic Plan should be monitored closely. Short term objectives and deliverables have to be defined in a yearly cycle and their progress should be monitored.

Also, a closer monitoring of seed fund investments is warranted. Specifically, comparisons are needed of SBAC scores assigned to the various projects, with resulting publications and follow-up grant applications. This will allow understanding of seed fund success/failure factors and a better 'targeting' of seed funds.

Priorities: Short Term, Long Term

Based upon the previous consideration, the following short term (1-2 years) and long term (3-5 years) priorities can be formulated

Short term priorities

Develop and implement a Visibility and Dissemination ('PR') policy, i.e. a communication plan.

Come up with a regular evaluation cycle of EC activities.

Formulate a leadership development strategy for EHDN committees that assures continued future membership commitment and diversity ('rejuvenation policy')

Establish a Science Coordination Committee, a Think Tank, and define its mode of operation. Have it generate novel research ideas, collaborations with SBAC to endorse projects and trials, and evaluate completed projects and trials.

Continue the Fellowship Exchange Programme; try to expand it by finding external partners, e.g. MDS.

Long term priorities

Re-energize working groups; establish closer ties, collaboration and dialogue.

Bring EHA membership deeper into EHDN's organization; organize discussions with EHA members on developments and directions.

Establish ties to other rare diseases networks.

Position SCC and CTTF as entries for companies into the network.

Get the message out that EHDN is willing to help members obtain international funding.