Leibniz-Gemeinschaft

Der Senat

17. Juli 2014

Stellungnahme zum Deutschen Diabetes-Zentrum (DDZ) – Leibniz-Institut für Diabetesforschung an der Heinrich-Heine-Universität Düsseldorf

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Vorbemerkung

Die Einrichtungen der Forschung und der wissenschaftlichen Infrastruktur, die sich in der Leibniz-Gemeinschaft zusammengeschlossen haben, werden von Bund und Ländern wegen ihrer überregionalen Bedeutung und eines gesamtstaatlichen wissenschaftspolitischen Interesses gemeinsam gefördert. Turnusmäßig, spätestens alle sieben Jahre, überprüfen Bund und Länder, ob die Voraussetzungen für die gemeinsame Förderung einer Leibniz-Einrichtung noch erfüllt sind.[1]

Die wesentliche Grundlage für die Überprüfung in der Gemeinsamen Wissenschaftskonferenz ist regelmäßig eine unabhängige Evaluierung durch den Senat der Leibniz-Gemeinschaft. Die Stellungnahmen des Senats bereitet der Senatsausschuss Evaluierung vor. Für die Bewertung einer Einrichtung setzt der Ausschuss Bewertungsgruppen mit unabhängigen, fachlich einschlägigen Sachverständigen ein.

Vor diesem Hintergrund besuchte eine Bewertungsgruppe am 5. und 6. Dezember 2013 das DDZ an der Heinrich-Heine-Universität Düsseldorf. Ihr stand eine vom DDZ erstellte Evaluierungsunterlage zur Verfügung. Die wesentlichen Aussagen dieser Unterlage sind in der Darstellung (Anlage A dieser Stellungnahme) zusammengefasst. Die Bewertungsgruppe erstellte im Anschluss an den Besuch den Bewertungsbericht (Anlage B). Das DDZ nahm dazu Stellung (Anlage C). Der Senat der Leibniz-Gemeinschaft verabschiedete am 17. Juli 2014 auf dieser Grundlage die vorliegende Stellungnahme. Der Senat dankt den Mitgliedern der Bewertungsgruppe und des Senatsausschusses Evaluierung für ihre Arbeit.

1. Beurteilung und Empfehlungen

Der Senat schließt sich den Beurteilungen und Empfehlungen der Bewertungsgruppe an.

Das Deutsche Diabetes-Zentrum (DDZ) – Leibniz-Institut für Diabetesforschung an der Heinrich-Heine-Universität Düsseldorf widmet sich der Verbesserung von Prävention, Früherkennung, Diagnostik und Therapie des *Diabetes mellitus* und seiner Folgeerkrankungen sowie der Verbesserung der epidemiologischen Datenlage zu dieser Krankheit. Vor dem Hintergrund der weltweit steigenden Prävalenz verfolgt das DDZ damit in überzeugender Weise das Ziel, auf der Basis interdisziplinärer Forschungsansätze Beiträge zur Reduzierung der individuellen und gesellschaftlichen Belastungen durch den *Diabetes mellitus* zu leisten.

Wie in früheren Stellungnahmen zum Diabetes-Zentrum vom Senat erwartet, gelang dem DDZ in den letzten Jahren eine grundlegende organisatorische, strukturelle und wissenschaftliche **Neuausrichtung**. Eine wesentliche Grundlage für diese sehr positive Entwicklung war die erfolgreiche Besetzung der Position des Direktors mit einem international anerkannten Wissenschaftler (2008). Im Anschluss daran konnten 2011 und 2013 zwei weitere Leitungspositionen erfolgreich neu besetzt werden.

Seitdem wurde das **Gesamtkonzept** unter Betonung translationaler Forschungsansätze schlüssig weiterentwickelt, so dass die Arbeiten nunmehr Aspekte der Grundlagenforschung überzeugend mit Fragen der klinisch-experimentellen sowie epidemiologischen

[1] Ausführungsvereinbarung zum GWK-Abkommen über die gemeinsame Förderung der Mitgliedseinrichtungen der Wissenschaftsgemeinschaft Gottfried Wilhelm Leibniz e. V.

Forschung verbinden. Mit großem Erfolg griff das DDZ dabei hochrelevante Themen der Diabetesforschung auf, u. a. in den Bereichen Energiestoffwechsel, Betazellbiologie, Gesundheitsökonomie und experimentelle Mausgenetik. Sie werden übergreifend und interdisziplinär durch die DDZ-Abteilungen, die als „Institute" bezeichnet werden, sowie durch neu eingerichtete Arbeits- und Nachwuchsgruppen bearbeitet. Empfehlungsgemäß stärkte das DDZ seine Patientenkollektive, die einen Kristallisationspunkt der Kooperation zwischen den Instituten und mit externen Partnern bilden. Das DDZ ist national und international mittlerweile deutlich sichtbar. Der Senat empfiehlt, die angestoßenen Veränderungsprozesse in den kommenden Jahren weiter voranzutreiben und damit die vom DDZ bereits erreichte Position als ein nationales Referenzzentrum für klinische Diabetesforschung langfristig zu festigen und auszubauen.

Die **Arbeitsleistungen** der vier Institute des DDZ und einer Forschergruppe (Paul-Langerhans-Gruppe) werden in zwei Fällen als „sehr gut bis exzellent" und in zwei Fällen als „sehr gut" eingeschätzt. In einem Fall werden „gute bis sehr gute" Leistungen erbracht. Der Senat begrüßt den vom Bundesministerium für Gesundheit (BMG) geförderten Aufbau eines Nationalen Informationszentrums für Diabetes als ein für den Beratungs- und Informationsauftrag des DDZ wesentliches Instrument und empfiehlt, dieses Zentrum weiterzuentwickeln und finanziell nachhaltig zu sichern.

Die **Kooperation** des DDZ mit der Heinrich-Heine-Universität (HHU) Düsseldorf im Rahmen von Forschung und Lehre ist sehr überzeugend. Die gemeinsame strukturierte Förderung von Promovierenden wurde deutlich intensiviert. Mit dem Universitätsklinikum Düsseldorf bestehen ertragreiche Verbindungen, die dem DDZ u. a. den für seine Forschungsarbeiten notwendigen Zugang zur stationären Patientenversorgung ermöglichen. Als Partner im Leibniz-Forschungsverbund „Gesundes Altern" engagiert sich das DDZ aktiv in der Leibniz-Gemeinschaft. Mit großem Erfolg beteiligt es sich am Deutschen Zentrum für Diabetesforschung (DZD e. V.). Der Senat begrüßt, dass es dem DDZ gelungen ist, eine federführende Rolle innerhalb des DZD einzunehmen und sich weiter zu profilieren.

Der **Anteil von Wissenschaftlerinnen** mit Leitungsaufgaben am DDZ ist zu gering. Der Senat erwartet, dass das Zentrum seine Anstrengungen zur aktiven Anwerbung exzellenter Wissenschaftlerinnen unter Beachtung der aufgrund des Kaskadenmodells festgelegten Zielquoten verstärkt.

Die **Mittel** der institutionellen Förderung sind auskömmlich. Der Senat begrüßt die in der Vergangenheit erreichten Steigerungen der eingeworbenen Drittmittel, empfiehlt jedoch, das Portfolio zu diversifizieren und dabei insbesondere den Anteil von Mitteln der EU und der DFG weiter zu steigern. Das DDZ verfügt über eine beeindruckende **Ausstattung** im Labor-, Tier- und klinisch experimentellen Bereich. Die im Grundsatz schlüssigen Überlegungen zur Anschaffung eines Hochfeld-MR-Tierscanners sollten konkretisiert und Möglichkeiten ihrer Umsetzung gemeinsam mit den Gremien geprüft werden.

Wissenschaftlicher Beirat und Aufsichtsgremium nehmen ihre jeweiligen Aufgaben engagiert wahr. Beide **Gremien** haben das Zentrum bei der erforderlichen Neuausrichtung in den vergangenen Jahren mit großer Sorgfalt unterstützt.

Abschließend hält der Senat fest, dass sich das Deutsche Diabetes-Zentrum in den letzten Jahren mit deutlich gesteigerten wissenschaftlichen Leistungen, den weiter ausgebauten Kohorten und Patientenkollektiven sowie ertragreichen Kooperationen zu einem auch im Ausland wahrgenommenen Referenzzentrum der Diabetesforschung entwickelt hat. Das DDZ erfüllt die bei den letzten beiden Evaluierungen vom Senat formulierten Erwartungen. Es bearbeitet eine eindrucksvolle Bandbreite hochrelevanter Aufgaben, deren Durchführung an einer Hochschule in dieser Form nicht möglich ist. Eine Eingliederung des DDZ in eine Hochschule wird daher nicht empfohlen. Das DDZ erfüllt die Anforderungen, die an eine Einrichtung von überregionaler Bedeutung und gesamtstaatlichem wissenschaftspolitischem Interesse zu stellen sind.

2. Zur Stellungnahme des DDZ

Der Senat begrüßt, dass das DDZ beabsichtigt, die Empfehlungen und Hinweise aus dem Bewertungsbericht bei seiner weiteren Arbeit zu berücksichtigen.

3. Förderempfehlung

Der Senat der Leibniz-Gemeinschaft empfiehlt Bund und Ländern, das DDZ als Einrichtung der Forschung und der wissenschaftlichen Infrastruktur auf der Grundlage der Ausführungsvereinbarung WGL weiter zu fördern.

18 November 2013

Annex A: Status Report

German Diabetes Center (DDZ), Leibniz Institute for Diabetes Research at Heinrich Heine University Düsseldorf

Contents

1. Structure, Tasks and Institutional Environment

Development and Funding

In 1965, the German Diabetes Research Association founded the "Diabetes Research Institute" (*Diabetes-Forschungsinstitut*, DFI), which was renamed in July 2004 as German Diabetes Center (Deutsches Diabetes-Zentrum, Leibniz Center for Diabetes Research DDZ. In 1977, DDZ became a member institution of the "*Blaue Liste*"[1]. Since then, 50 % of its institutional funding has been provided by the Federation (*Bund*) and 50 % by the state of North Rhine-Westphalia and the other *Länder*.

DDZ was evaluated by the Senate of the Leibniz Association in 2003, 2007 and 2009. On the basis of the Senate's recommendations as well as a joint statement by the responsible departments at Federal and *Länder* level in February 2010, the Joint Science Conference determined that DDZ still met the requirements for joint funding. At the same time, the Conference scheduled the next review to take place in 2014.

Responsible department at *Länder* level: Ministry of Innovation, Science and Research of North Rhine-Westphalia (MIWF), Düsseldorf

Responsible department at Federal level: Federal Ministry of Health (BMG), Bonn

Legal form and organisation

The institution is a registered association named German Diabetes Research Association ("*Deutsche Diabetes Forschungsgesellschaft e. V.*"). According to its statutes the association's general purpose lies in the advancement of science and research as well as the public health service. The association works to execute and promote research within the field of diabetes by operating DDZ. The organs of the association are as follows:

The **General Assembly** currently has sixteen members, including representatives of the relevant departments at Federal as well as at *Länder* level. The General Assembly, amongst others, deals with the annual financial statement, the prospective business plan as well as the report of the Executive Board on the Association's activities.

The **Board of Trustees** decides on all fundamental and strategic matters relating to the Association. It determines the principles on which the activities of DDZ are based. Furthermore, it elects and supervises the Executive Board. Currently, the Board of Trustees has nine members, *i.e.* the rector of Heinrich Heine University Düsseldorf, ministerial representatives, medical experts and the Chairman of the Scientific Advisory Board.

The Scientific and Administrative Directors constitute the **Executive Board**, which operates the business of the Association and the Center according to the Association's statutes as well as the decisions of the General Assembly and Board of Trustees. The Scientific Director functions as Chairman of the Board.

The **Scientific Advisory Board** (SAB) consists of at least seven (currently eleven) members who are elected by the General Assembly upon proposal by the directors of DDZ's institutes as well as the Executive Board. The term of office is six years. Re-election is

[1] The association of the members of the "*Blaue Liste*" (blue list) subsequently became the Leibniz Association.

feasible. The SAB's function is, amongst others, to advise DDZ on all scientific matters and to regularly assess DDZ's achievements and future plans.

Mission and tasks

According to its statutes, the primary mission of DDZ is to contribute to the reduction of the individual and societal burden of *diabetes mellitus* by transdisciplinary research. Its research concept is to combine molecular and cell biology research with clinical, epidemiological, and health service research. The results are translated into diabetes care, in particular by improving the early detection, prevention, and treatment of diabetes and its sequelae. In addition, DDZ provides comprehensive epidemiological data and detailed information on *diabetes mellitus* for the public as well as for experts within the health care system.

Research structure

DDZ consists of **five research units** (four institutes and the Paul Langerhans Group), complemented by **four core facilities** and **two staff units**. Horizontal to this DDZ has structured its research in **four research programmes**.

National and international scientific environment

According to DDZ, its unique feature resides in its transdisciplinary approach from basic to applied research both in type 1 and type 2 diabetes and its complications as well as in its close link to patient care at Düsseldorf University Hospital (UKD). Although several **German universities** have diabetes research groups, *e.g.* the universities of Heidelberg, Lübeck, Leipzig, Bremen, Hannover, Bochum and the Max Planck Institute in Cologne, none of these utilise a similar comprehensive approach to that at DDZ.

Important national reference institutes include the German Research Center for Environmental Health (Helmholtz Zentrum München, HMGU), the Institute for Diabetes Research and Metabolic Diseases at the University of Tübingen, the German Institute of Human Nutrition (DIfE Potsdam-Rehbrücke) and the Paul Langerhans Institute at Technical University Dresden – all of which are member institutes in the predominantly federal-funded network, **German Center for Diabetes Research** (*DZD e. V., Deutsches Zentrum für Diabetesforschung*).

In Europe, the **Institute of Metabolic Science Cambridge** and the **Oxford Diabetes Center** have broad interdisciplinary research programmes similar to that at DDZ, ranging from genes to clinical services. The **Steno Diabetes Center**, now owned by the pharmaceutical industry, has covered basically all aspects of type 1 and type 2 diabetes and its complications with similarities to DDZ. According to DDZ, various other European programmes perform excellent diabetes research, but none has a comprehensive research approach similar to that at DDZ.

On an international level beyond Europe, a few scientific institutions have a similar trans-disciplinary approach such as the **Joslin Diabetes Center**, affiliated with Harvard Medical School (Boston, MA), covering all main aspects of diabetes research, and the **Baker IDI Heart and Diabetes Institute** (Melbourne), which has refocussed from car-

diovascular to diabetes research over the last years. In addition, several medical schools maintain research groups, mostly addressing specific aspects of diabetes, *e.g.* the **University of Texas** at San Antonio, **Yale Diabetes Center, Mayo Clinics, Albert Einstein Diabetes Research Center**, and the **University of California**, San Diego.

National interest and justification for funding as a non-university institution

DDZ addresses one of the leading chronic diseases, *diabetes mellitus*, which affects more than six million individuals in Germany. Following its four research programmes, DDZ not only conducts independent scientific projects, but also makes its results available to German Federal and *Länder* authorities, to patients as well as to the general public. According to DDZ, the transdisciplinary approach with clinical studies, databases and biobanks can only be achieved and maintained by a long-term research strategy involving multiprofessional teams, which cannot be done in a university setting.

In its own view, the supra-regional significance of DDZ results from its leading or collaborative role in national and international networks and consortia. DDZ is a transdisciplinary and inter-professional institution with a unique translational profile and facilities for basic sciences, clinical research, epidemiology, and health services research. DDZ initiated and conducts the long-term prospective German Diabetes Study (GDS) and maintains the registers and biobanks (T1DM-NRW Register, T1DM biobank) for type 1 and type 2 diabetes – thus providing a unique resource for German diabetes research. DDZ is also responsible for the diabetes-related analyses of the long-term KORA study (Cooperative Health Research in the Augsburg Region) and participates in the planning, recruiting and performing phenotyping of the National Cohort (*Nationale Kohorte*). Along with the Helmholtz Zentrum München – German Research Center for Environmental Health (HMGU) and the German Institute of Human Nutrition (DIfE), DDZ forms the German Diabetes Mouse Clinic with its long-term agenda to identify genes related to diabetes in polygenic mouse models. To fulfil its commitment to transfer science to routine care, the areas of health services research, health economics and patients' perspectives have been continuously expanded since the last evaluation. As a result of its supra-regional significance, DDZ is also an essential partner in various national research networks, international and global consortia in the field of diabetes and related diseases.

2. General concept and profile

Development of the institution since the last evaluation

DDZ's aims are to identify individual and population-based risk factors to better understand the pathogenesis and to develop novel approaches for the prediction as well as for the personalised prevention and treatment of diabetes with a focus on type 2 diabetes and its related complications.

In order to implement its mission, DDZ's current structure is composed of **four institutes** (*vertical structure*), which altogether consist of **eleven research groups** complemented by **four core facilities**. In the past, DDZ established two so-called **Paul Langerhans Groups**, one of which was transformed into a fourth institute in 2013. The animal

laboratory and the National Diabetes Information Center are **staff units** at DDZ (cf. Appendix 1).

In order to structure its research, DDZ has developed a long-term research concept comprising **four research programmes** (*horizontal structure*), which have been refined in the past in accordance with previous recommendations by the Senate of the Leibniz Association. According to DDZ, the programmes address issues with the overall translational and transdisciplinary objective of uncovering the pathogenic, clinical and epidemiological features underlying the variability of the disease complexity currently summarised as *diabetes mellitus*. This approach aims to identify strategies for detecting risk as well as the preventive and patient-oriented treatment of *diabetes mellitus* and its complications.

- PROGRAMME A: "Identification of new pathogenic mechanisms and molecular target structures in *diabetes mellitus*"
- PROGRAMME B: "Investigation of the development, progression, and sequelae of *diabetes mellitus*"
- PROGRAMME C: "Investigation of the epidemiological foundations and development of models for the prevention and care of *diabetes mellitus*"
- PROGRAMME D: "Determination of the individual courses of disease of *diabetes mellitus* in adults (German Diabetes Study (GDS)"

In addition to the advancement and focussing of the research programme, DDZ has undergone further **structural changes** since 2009:

- **New directors**: In March 2011, a new director of the Institute for Clinical Biochemistry and Pathobiochemistry was appointed jointly with Heinrich Heine University Düsseldorf. The new head refocussed the research programme on the genetic and molecular mechanisms in mouse models of insulin resistance and diabetes (cf. chap. 3.2). Also, in October 2013 a new director of the Institute for Biometrics and Epidemiology was appointed (cf. chap. 3.3).
- In order to extend its research program, in 2011 DDZ initiated two independent subdivisions, the **Paul Langerhans Groups** for Integrative Physiology and for Beta Cell Biology, the latter being transferred into the Institute for Beta Cell Biology in 2013 (cf. Ch. 3.4 and 3.5). Also, starting in 2009, DDZ established three **Junior Research Groups**.
- In 2009, the federal-funded German Center for Diabetes Research (*Deutsches Zentrum für Diabetesforschung* – ***DZD*** *e. V.*) was founded as a network and joint programme of diabetes research in Germany. DDZ became the lead partner for the **German Diabetes Study** (GDS) and functional diabetes phenotyping. Also, DDZ became a partner in other programmes, *e.g.* the German Diabetes Mouse Clinic, epidemiology, and beta cell biology.
- In 2011, DDZ was chosen as a study centre for the **National Cohort** (*Nationale Kohorte*), a nationwide cohort study (200,000 participants, 10,000 of which will be re-

cruited in Düsseldorf). During the observation period of 20 years, incident cases of cardiovascular diseases, cancer, type 2 diabetes and dementia will be ascertained.

Results

The primary focus of **publication activity** at DDZ is on original articles in high-ranking, peer-reviewed international journals in the field of diabetes research or related areas. In addition, cumulative results and expertise are also contributed to peer-reviewed international textbooks. In the period 2010–2012, DDZ scientists published 91, 123 and 124 peer-reviewed **original and review articles** respectively (cf. Appendix 2). Between 2010 and 2012, the annual cumulative impact factor of peer-reviewed publications rose from 490 to 851.

Altogether, DDZ scientists have been invited to hold approx. 350 talks at national and international level since 2010. All in all, they gave more than 300 oral and poster presentations at conferences.

In order to study diabetes comprehensively DDZ runs various **clinical cohorts and registers**, the main cohort being the German Diabetes Study (GDS) – a prospective study on the course of diabetes in adult patients with recently diagnosed diabetes.

DDZ also contributes **to collaborative and genetic and molecular research** within the German Mouse Clinic at the Helmholtz Zentrum München/Neuherberg in cooperation with the DIfE Potsdam-Rehbrücke, providing instrumentation and resources for metabolic phenotyping of rodent models for diabetes. Moreover, DDZ has established a mouse clamp unit, which allows detailed metabolic studies using stable isotope technology. For clinical-experimental studies, DDZ provides service and training in methods for invasive and non-invasive studies in human metabolism. Furthermore, DDZ service platforms advise and collaborate with national and international partners.

DDZ provides web-based **information platforms** for the dissemination of information on diabetes and associated complications, targeting patients and the general public, including quality assured patient information. Furthermore, DDZ offers expertise on diabetes epidemiology to large national and international epidemiological studies and agencies as well as in various consultancy services for policy-makers.

To further advance **knowledge and technology transfer,** in 2006, DDZ established structures for filing inventions and patenting research results in cooperation with an external patent-marketing agency. Between 2010 and 2012, three patent applications and one invention were filed (cf. Appendix 2).

Academic events and public relations

Since 2010, DDZ has organised various conferences, symposia and workshops addressing a multitude of stakeholders (scientists, diabetologists, patients, medical experts etc.) on an annual basis. The main academic events included the “Düsseldorf-Maastricht Diabetes Day”, an international “Rainbow Proteomics Workshop”, the “Jühling Symposium” and the “Kaiserswerther Diabetes Patient Care Symposium”.

DDZ's press office serves as the main contact partner for journalists and experts, and regularly posts recent developments, scientific news and results on DDZ's website. It is responsible for the organisation of events and meetings as well as media coverage.

Strategic work planning for the next few years

DDZ plans to maintain its **mid-term research focus areas** along the lines of the programmes A–D (see above). Based on these programmes, it intends to pursue strategic goals, which have been identified to combine the different expertise in the research units and to allow for further strategic interaction between the programmes. To facilitate the development of new research topics, DDZ intends to establish at least two Junior Research Groups which will later be integrated in the research programme.

Also, DDZ plans to continue its participation in comprehensive programmes, studies and surveys (*e.g.* German Center for Diabetes Research, National Cohort). Moreover, it has drawn up plans to further develop its strategy to improve disseminating relevant research results to the public (*e.g.* web-based information platforms).

As a **long-term research perspective**, DDZ will pursue the strategy of identifying the individual risk of diabetes and its complications and further strengthen its efforts for a better understanding of the mechanisms influencing its progression and for testing concepts for personalised treatment of the disease. Thus, DDZ plans to emphasise the following long-term research areas:

- to identify susceptibility genes for diabetes risk through experimental and molecular genetics using mouse models and patient cohorts, and to elucidate the molecular mechanism of interactions between inherited and acquired factors (genes, lifestyle, environment) implicated in the onset and progression of diabetes
- to evaluate the roles of cellular energy metabolism, inflammation, blood vessel-derived and cardiovascular-related mechanisms and multi-organ crosstalk in the susceptibility to and during the course of experimental and human diabetes in order to identify novel targets for personalised prevention and biomarkers of the individual response to treatments
- to analyse risk factors relevant to public health that contribute to the development of diabetes and influence its progression, and to monitor changes in the clinical and cost effectiveness of diabetes care from the patients' perspective
- to enlarge the DDZ cohorts by including diabetes risk groups and to design an independent intervention study starting from the German Diabetes Study and investigating novel drug targets that have been developed at DDZ

Appropriateness of facilities, equipment and staffing

In 2012, DDZ's **total revenue** was € 16.4 million, including € 11.0 million (69 %) institutional funding and € 4.9 million (31 %) from **project funding grants**. Of prime importance were funds received from the German Center of Diabetes Research (*DZD e. V.*, € 1.5 million on average since 2010), followed by Federal/*Länder* funds, industry funds and

German Research Foundation (DFG) funds (cf. Appendix 3). On average, project funds contributed approx. 25 % of DDZ's total revenue in 2010–2012.

Since the last evaluation, DDZ substantially improved its **infrastructure** and **facilities**, especially in connection with the recruitment of the directors of the Institute for Biochemistry and Pathobiochemistry and the Paul Langerhans Group for Beta Cell Biology in 2011 and 2012, respectively. Furthermore, since 2009, the endowments for DDZ's director were invested to provide for state-of-the-art equipment for clinical-experimental studies.

Also, in 2008, the Executive Board developed a stepwise mid-term plan to improve specific research facilities:

- a study centre for the National Cohort (*Nationale Kohorte*, to be completed in 2013)
- labs for the new Institute for Beta Cell Biology (formerly Paul Langerhans Group for Beta Cell Biology) to be set up and equipped in 2013
- an exercise training facility (to be completed in 2014)
- clinical-experimental labs for complex metabolic studies including tissue biopsies in humans (to be completed in 2015)

Whilst adequate in the last years, the recruitment of two head scientists in 2011 and 2012 made it necessary to extend the **animal facilities** (esp. mouse maintenance). According to DDZ, equipment and methodologies for advanced phenotyping will be further expanded.

Overall, in DDZ's assessment, its facilities, particularly space and basic equipment, are appropriate to run the research programmes.

3. Subdivisions of DDZ

3.1 Institute for Clinical Diabetology (Roden)

(32.8 FTE[2], thereof 11.0 FTE Research and scientific services, and 17.4 FTE Service staff)

The Institute for Clinical Diabetology comprises **five research groups** and **one junior research group**:

- Energy metabolism (Roden)
- Inflammation (Herder)
- Immunomodulation (Burkart)
- Neuropathy (Ziegler)
- Nutrition (Müssig)
- Metabolic imaging (Hwang; junior research group).

Also, **two service platforms** are associated with the institute.

The Institute for Clinical Diabetology investigates the development and sequelae of *diabetes mellitus* by (1) studying systematic pathomechanisms in *diabetes mellitus* and its

[2] FTE = Full-time equivalent

complications, addressing abnormal energy metabolism (mitochondrial function and lipid storage) and (2) by studies of biomarkers allowing for individualised prevention, early detection and treatment of *diabetes mellitus* and its complications. In the past, the institute developed a programme on novel methods of clinical phenotyping in patient cohorts.

Following the appointment of the new director in 2008, in recent years, the institute has developed its research programme from an immunologically oriented focus emphasising type 1 diabetes into an integrated programme on both basic and clinical aspects of early alterations in or leading to insulin resistance, type 2 diabetes and selected complications. Hence, the institute addresses cellular mechanisms underlying insulin resistance focussing on tissue-specific energy metabolism, including mitochondrial function and lipid deposition, and on its interaction with innate immune processes that promote diabetes. In particular, hypotheses are generated from cohort studies, tested in animal models of diabetes, and translated to models of acute and chronic insulin resistance in humans. To this end, researchers at the institute established and validated novel invasive methods such as high-resolution respirometry in tissue samples to directly assess muscle and liver metabolism in mice and humans. In parallel, non-invasive methods for the assessment of tissue specific metabolic flux rates such as glucose and energy metabolism were established and combined with stable isotope dilution techniques for extensive phenotyping of subgroups of national cohorts.

Furthermore, members of the institute study the association between mediators of inflammation and the risk of type 2 diabetes and related complications. Also, the research strategy on the early detection and characterization of diabetes-related neuropathies was redirected to focus on establishing novel methods to quantify peripheral nerve structure and on the identification of new markers for neuropathy in skin and stomach biopsies and validation of surrogate measures such as corneal confocal microscopy.

Since the last evaluation, the main research results reported by the research groups lay in the fields of energy metabolism (*e.g.* alterations of ATP turnover in muscle and liver in different states of human insulin resistance, lipid-mediated insulin resistance in humans, relative roles of mitochondrial function and inflammatory pathways) and the individualised prediction of diabetes and its complications (*e.g.* combined analysis of pro- and anti-inflammatory biomarkers). Also, new methods were established and adapted for use on clinical MR scanners, *e.g.* to quantify body fat content and distribution.

In the near future, the institute plans to

(1) Strengthen its efforts to elucidate the interaction of energy metabolism with inflammatory and immunomodulatory pathways (Toll-like receptors, stress signals). To this end, methods for tracing tissue-specific kinetics of fatty acids and amino acids will be established. Also, starting from ongoing studies, a human biobank will be established aiming at comprehensive characterisation and tissue-specific difference of the metabolome and mitochondrial metabolism.

(2) Intensify its strategy for improving the prediction of risk of type 2 diabetes and associated complications, e.g. by investigating associations between biomarkers of

subclinical inflammation and conditions of (pre)diabetes and diabetes complications.

(3) Continue to optimise current imaging technologies for future studies.

In the period under review, members of the institute published 38 (2010), 56 (2011), and 49 (2012, plus 14 accepted for publication) original articles and 8, 13, and 5 (+3) review articles in peer-reviewed journals respectively. Revenues from project grants rose from € 1.95 million to € 2.52 million. Between 2010 and 2012, seven doctoral candidates received their degrees and two members qualified as professors.

Service platform 'Clinical Research Center' (CRC)

(18.7 FTE, thereof 6.3 FTE Research and scientific services and 11.4 FTE Service staff)

As a service platform, CRC coordinates clinical studies and offers expertise and training in examination techniques, also to external partners. Its main task resides in the recruitment and performance of all clinical tests for the German Diabetes Study (GDS). In addition, CRC organises and operates other clinical studies as well as phase-2 and -3 trials at DDZ.

In recent years, the main cohort of DDZ, the German Diabetes Study, was further enlarged to now altogether 636 patients having their baseline examination and 210 patients having their 2-year or 5-year follow-up examinations done in December 2012.

In future, CRC will intensify its work on the inclusion of new patients and patient follow-up at DDZ and orchestrate patients' recruitment at cooperating centres within the *DZD e. V.* In particular, it is planned to elucidate the variability of patients' responses to tailored interventions in overt diabetes and to identify factors contributing to the individual time course of diabetes development. The main objectives will be, *e.g.*, (a) the identification of biomarkers related to alterations in the energy metabolism and genetic susceptibility to the risk of diabetes and diabetes related complications, (b) the development and implementation of techniques to improve phenotyping, (c) the analysis of gene expression patterns, and (d) the characterisation of the individual responsiveness of diabetes patients to lifestyle intervention.

Service platform 'Technical Laboratory'

The Technical Laboratory was introduced to ensure high-quality, inhouse laboratory analyses of hormones, metabolites and screening parameters. It performs stable isotope analyses (gas chromatography mass spectrometry, GCMS) and selected metabolomics measurements for DDZ as well as for external partners. In 2010, the institute initiated the installation of a whole body 3-T MR scanner and implemented state-of-the-art techniques and methods, which, according to DDZ, are instrumental in clinical research.

3.2 Institute for Clinical Biochemistry and Pathobiochemistry (Al-Hasani)

(27.4 FTE, thereof 11.5 FTE Research and scientific services, and 12.4 FTE Service staff)

The Institute for Clinical Biochemistry and Pathobiochemistry has **one research group** (Pathobiochemistry, Al-Hasani) and **one junior research group** (Signal transduction, Ouwens). **Two service platforms** are associated with the institute.

The Institute for Clinical Biochemistry and Pathobiochemistry investigates the molecular basis of the onset and progression of obesity, insulin resistance and type 2 diabetes in order to improve prevention, prediction and therapy of diabetes. A strong focus has been the identification and molecular analysis of adipocyte-derived factors that regulate whole-body metabolism, and cardiovascular function. New facilities for performing experimental mouse genetics and detailed metabolic phenotyping of mouse models for obesity and diabetes have been established.

Scientists at the institute have taken part in interdisciplinary research activities to gain new insights into the pathophysiology of diabetes and its related complications. Major achievements include the discovery and validation of biomarkers for diabetes and cardiovascular complications by a systematic proteome-wide analysis of fat cell-derived factors. In addition, new mechanisms underlying the development of lipid-induced insulin resistance in human subjects have been identified.

As of March 2011, the new director introduced work on *in vivo* models of insulin resistance and diabetes into the research strategy. In particular, state-of-the-art technologies and instrumentation for physiological characterization of mouse models as well as experimental mouse genetics have been implemented as tools to identify novel risk genes and relevant gene/gene and gene/environment interactions in obesity and diabetes. Furthermore, methods such as the characterization of intact isolated mouse skeletal muscle have been established for metabolic studies on glucose and lipid metabolism of rodent models. These facilities are complemented by service platforms for mass spectroscopy-based proteome analysis and morphological imaging.

In the near future, the institute will place particular emphasis on the following key aspects:

(1) identification of new diabetes risk gene variants and gene/environment interactions through the large-scale ‘collaborative cross’

(2) characterization of modulators of insulin action and cardiovascular complications in type 2 diabetes using unique cell types and animal models for the disease

(3) understanding the contribution of susceptibility gene variants for diabetes in disease progression

(4) further advancement in comprehensive metabolic phenotyping of mouse models for diabetes using novel instrumentation and methodologies

In the period under review, members of the institute published 15 (2010), 22 (2011), and 24 (2012) original articles in peer-reviewed journals. In the same period, a total of nine review articles in peer-reviewed journals were published. Revenues from project

grants ranged from € 39 k (2011) to € 190 k in 2010. Between 2010 and 2012, three doctoral candidates received their degrees.

Service platform 'Cellular Morphology'

This service platform was created in 2011 and is involved in various DDZ research projects requiring morphological and/or ultrastructural information. This includes but is not limited to routine histology analysis of tissues from rodent diabetes models, analysis of human tissue biopsy material and phenotyping of subcellular structures such as mitochondria and islet secretory granules.

Service platform 'Proteome Analysis'

The service platform 'Proteome Analysis' was also established in 2011. It provides access to advanced proteome (DIGE/Mass spectroscopy) and biomarker analysis of cells/ tissues from rodent diabetes models and clinical samples. The unit is also involved in genetic analyses and is establishing a biobank for the German Diabetes Study cohort.

3.3 Institute for Biometrics and Epidemiology (Giani / Kuß)

(31.2 FTE, thereof 19.5 FTE Research and scientific services, and 8.4 FTE Service staff)

The Institute for Biometrics and Epidemiology consists of **three research groups:**

- Epidemiology (Rathmann)
- Biometrics (Finner)
- Health Service Research and Health Economics (Icks)

After the retirement of the institute's head in July 2013 a new director assumed office in October 2013 (cf. chapter 4).

The institute performs research on the epidemiology of diabetes and on diabetes prevention and care. This comprises the assessment of diabetes prevalence, incidence and risk factors, and the development of prognostic models of *diabetes mellitus* and its complications as well as the improvement of statistical methods for the design and analysis of epidemiologic studies in diabetes research.

To this end, the institute has established its own cohorts (type 1 and type 2 diabetes incidence register in children and young adults, paediatric biobank) and has also used external epidemiological platforms to derive population-based estimates on diabetes incidence and prevalence. This data has contributed to international consortia for type 1 diabetes epidemiology, for type 2 diabetes prediction, and meta-analyses of genome-wide association studies on glycemic and metabolic traits. Also, it is actively involved in the National Cohort. Methodological research topics at the institute address multiplicity issues with special focus on high dimensional (-*omics*) data and reproducibility.

Recently, the institute initiated a new research group on health service research and health economic evaluation of prevention and care of *diabetes mellitus*. In this group the clinical and cost effectiveness of diabetes prevention and treatment in daily routine care are evaluated from the patient's point of view. Novel patient reported outcomes like patients' information needs and participation preferences are analysed, as well as trends

in risks of patient-relevant outcomes (*e.g.* amputations), and efficiency, including innovative measures like patient time cost.

Most of the institute's results derived from analyses of its population-based cohorts and in-house diabetes registries. Members of the institute were able to demonstrate an increase in the incidence of type 1 diabetes in children and young adults in recent years whilst the incidence of type 2 diabetes in these age groups was much lower and has not changed in the last ten years. Intensified investigations in physiological, sociological, societal as well as environmental conditions lead to new insights into the onset and development of diabetes. Also, researchers at the institute initiated a meta-analysis of regional population-based cohorts in Germany, recording for the first time regional disparities in type 2 diabetes prevalence in Germany.

In the field of health service research and health economics, the institute succeeded in evaluating the incidence of all St. Vincent declaration outcomes and of mental comorbidity in the diabetic and the non-diabetic populations as well as mortality after these events. On a methodological basis, the institute developed a series of new methods and results with regard to multiplicity issues.

The main aims of the institute for the next few years include, *e.g.*:

- surveillance of the incidence and course of diabetes in young age groups
- identification of Public Health relevant risk factors (*e.g.* socioeconomic indicators, environmental factors) that contribute to the development of diabetes and influence the course of the disease
- investigation of the clinical and cost effectiveness of diabetes prevention and treatment in daily routine care, particularly considering the patients' perspective
- development and application of multiple tests for high-dimensional data

In the period under review, members of the institute published 31 (2010), 41 (2011), and 74 (2012, including 18 papers accepted for publication) original articles in peer-reviewed journals. In the same period, 17 review articles appeared in peer-reviewed journals. On average, the institute received approx. € 635 k in revenue from projects grants. Between 2010 and 2012, four doctoral candidates received their degrees, one member of the institute qualified as a professor.

3.4 Institute for Beta Cell Biology (Lammert)

(formerly Paul Langerhans Group for Beta Cell Biology; transformed into an institute in July 2013; 2.0 FTE, thereof 2.0 FTE Research and scientific services)

The institute covers the field of pancreatic beta cells and vascular endothelial cells. The underlying working hypothesis is that within pancreatic islets, communication among beta cells, and between beta cells and endothelial cells, is essential for the physiological function, growth and survival of the islet. The research is focussed on proteins originally identified as being involved in neuronal cell-to-cell communication and survival as well as proteins involved in the interaction with vascular basement membrane.

In the past, the group revealed novel molecular mechanisms involved in the formation and growth of vessels. Also, it published methods to pharmacologically test the effects of small molecules on the developing vasculature.

In future, molecular signalling pathways involved in cell-to-cell communication of pancreatic beta cells and endothelial cells will be explored in more detail. A major focus will be on 'drugable' signalling pathways to identify drug targets for the treatment of type 2 diabetes and its micro-vascular long-term complications.

DDZ has cooperated with the head of the Institute of Metabolic Physiology in the Biology Department at Heinrich Heine University (HHU), Düsseldorf, since he was appointed to a W3 professorship. In addition to his professorship at HHU, he took over the position of head of the Paul Langerhans Group for Beta Cell Biology in January 2012.

Since its establishment in 2012, the group has published five original/review articles in peer-reviewed journals. One article appeared in another journal, another article was accepted for publication in 2012. The institute was able to raise funds in the amount of € 520 k in 2012. One doctoral candidate received a doctoral degree.

3.5 Paul Langerhans Group for Integrative Physiology (Eckel)

(9.1 FTE, thereof 3.8 FTE Research and scientific services and 1.8 FTE Service staff)

In 2011, the Paul Langerhans Group for Integrative Physiology was established in order to conduct translational research in the field of organ crosstalk and communication. The group addresses new topics like myokines and vasoactive compounds and has now established a unique platform of experimental settings to analyse organ crosstalk and its functional implications. The characterisation of adipokines and myokines regarding their functional role in adipose tissue, in skeletal muscle and in the vasculature is the main objective of the group. A new model aims at identifying novel molecular mechanisms of type 2 diabetes and represents, according to DDZ, a translational link between DDZ subdivisions.

In the recent past, proteomic profiling of the secretome of human adipocytes led to the description of many novel candidates that require further characterisation.

To better understand the crosstalk between skeletal muscle and adipose tissue in the context of physical exercise, an innovative model of contracting human skeletal muscle cells was established.

In future, the group will extend its research programme on bi-directional organ crosstalk and its functional implications for both disease-initiating and -preventing processes. Major future objectives are:

– The characterisation of DPP4 as a novel adipokine with cardiovascular effects, the breeding and metabolic phenotyping of the adipose tissue-specific DPP4 knockout mouse, and the measurement of DPP4 and other novel adipokines in different cohorts.

– To use an electrical pulse stimulation system to mimic different types of exercise training, to analyse novel myokines in clinical samples, and to establish novel myokines as markers of successful exercise intervention.
– To validate and characterise novel adipo-myokines as potential therapeutic targets with emphasis on the white to brown adipose tissue programming, to extend the metabolic phenotyping of "brite" adipocytes, and to analyse the signalling pathways regulating the brown programming in human preadipocytes.

Since its establishment in 2011, group members have published 20 original articles in peer-reviewed journals as well as five review articles in peer-reviewed journals. The group received project funds in the order of € 150 k (2011) and € 1 mill. (2012). Four doctoral candidates received their degrees.

3.6 Staff units

Animal Facility

(5.0 FTE, thereof 1.0 FTE Research and scientific services and 4.0 FTE Service staff)

This core facility builds the infrastructure for the breeding and phenotypic characterization of rodents and support for submission of animal ethics protocols. In addition to providing several mouse models of diabetes, obesity and lipid disorders, since 2011, the infrastructure has been extended for performing metabolic phenotyping, and dietary and exercise intervention studies. This was developed in parallel with CRC to facilitate the translation of results from rodents to patients and vice versa. The facility also contributes to the German Diabetes Mouse Clinic, the multicentric platform of *DZD e. V.* for conducting large-scale mouse studies in diabetes. The head of the animal facility is also acting animal welfare officer (*Tierschutzbeauftragter*) and responsible for compliance of animal work with the animal welfare laws. The experimental animal work is conducted by scientists and technicians from the different institutes and supported by animal caretakers.

In the future, the facility will continue to contribute to animal studies related to the pathogenesis of *diabetes mellitus*. Several new mouse models have been generated at DDZ and will be characterised further using resources located in the animal facility. A particular focus will be the establishment of new methods for non-invasive metabolic phenotyping and *in vivo* imaging technologies (11.7-T MR for small animals).

National Diabetes Information Center

(5.0 FTE, thereof 2.5 FTE Research and scientific services and 2.5 FTE Service staff)

The unit provides an information platform and an online service for patients, specialists and the general public offering information on *diabetes mellitus* and diabetes-related topics. In addition, it offers a web-based Diabetes Information Service, where patients and interested parties can address their queries on individual diabetes and diabetes-related topics to experts at DDZ.

Since its launch in 2009, the unit has dealt with more than 1,300 individual requests. On

average, the platform had more than 400,000 hits per month in 2011 and over 480,000 hits per month in 2012.

In future, the unit will continue to establish a broad, state-of-the-art information platform characterised by independent neutral and quality assured information on diabetes and related diseases. Further investigation and more detailed statistical analysis will make it possible to identify and close information gaps.

4. Collaboration and networking

Collaboration with universities

DDZ cooperates with **Heinrich Heine University Düsseldorf** (HHU) and **Düsseldorf University Hospital** (UKD).

Cooperation with HHU includes the joint selection of professors, the coordination of research and teaching, joint scientific events as well as scientific collaboration. Currently, nine senior scientists are professors at HHU, three at W3-level, two at C3/W2-level and four as adjunct professors. All positions at W3-level as well as one position at W2-level are financed directly by HHU (cf. Appendix 4).

Since 2010, four professors have been jointly appointed/selected with Heinrich Heine University (three W3, one W2), including a W3-professorship in the field of Biometrics, Epidemiology and Health Services Research in combination with the directorship of the Institute for Biometrics and Epidemiology (successor to Giani) in 2013. Also, a UKD senior scientist was appointed head of the former Paul Langerhans Group for Beta Cell Biology in 2012.

According to DDZ, its jointly selected/appointed professors, adjunct professors and other scientific staff continuously contribute to the bidirectional supervision of theses and teaching, the latter comprising courses as well as medical and methodological seminars. DDZ researchers also serve as guest/adjunct professors and contribute to curricular and post-graduate training at other universities.

Furthermore, researchers at DDZ are involved in a number of coordinated programmes, *e.g.* as coordinators of future focus areas at HHU ('Diabetes' and 'Health and Society') or project leaders of established collaborative research centres (SFBs), graduate schools and post-graduate courses.

Collaboration with other domestic and international institutions

DDZ reports that it has multiple collaborations with national and international research networks as well as individual institutions.

On the national level, DDZ is a partner in the **German Center for Diabetes Research** (*DZD e. V.*), providing one of three speakers and project leaders. This network links DDZ with the German Research Centre for Environmental Health (Helmholtz Zentrum München), the German Institute of Human Nutrition Potsdam (DIfE) and the universities of Tübingen and Dresden, with which DDZ also interacts in other programmes. Also, DDZ contributes to the **Competence Network Diabetes mellitus** (KKNDm – *Kompetenznetz*

Diabetes mellitus), which brings together universities and other institutions covering more than 20 projects in five areas (pre-clinical, biomarkers, cohorts/biobanks, intervention/treatment, epidemiology and health care research). Furthermore, together with the Leibniz Research Institute for Environmental Research Düsseldorf (IUF), DDZ is the local site of the nationwide research consortium of university and non-university partners, which form the **National Cohort** study (*Nationale Kohorte*).

DDZ collaborates with other **Leibniz** institutes under the Leibniz Competition (SAW) and the Leibniz Research Cluster "Aging", connecting 23 Leibniz institutes with projects focussing on age-related alterations.

On an **international level**, DDZ participates, and has participated, in several European research networks and projects, *e.g.* ADAPT ("Adipokines as Drug Targets to Combat Effects of Excess Adipose Tissue"). Senior scientists successfully applied for various work packages and partnerships or were members of steering committees in the past. Altogether, DDZ acquired € 54 k (2010), € 5 k (2011) and € 448 k (2012) from **EU** funds.

DDZ collaborates with research groups at other non-university partners such as the National Institute for Health and Welfare (Helsinki, Finland) and the Baker IDI Heart and Diabetes Institute (Melbourne, Australia). The center also collaborates with Harvard Medical School (Boston, USA), the Howard Hughes Institute at Yale University (New Haven, USA), the National Institute of Health (Bethesda, USA), the Karolinska Institute (Stockholm, Sweden) and San Raffaele Scientific Institute (Milan, Italy).

In the period 2010–2012, international activities resulted, according to DDZ, in 121 original publications from bilateral cooperation, 54 original publications from consortia and 25 reviews.

Altogether, between 2010 and 2012, DDZ hosted 24 guest research visits, eleven of which lasted longer than three months. At the same time, five DDZ researchers of DDZ stayed at other institutions.

Other collaborations and networks

DDZ has contracts with industrial partners mainly for basic research in diabetes, developing methodologies as well as designing and performing clinical trials on the treatment of type 1 and type 2 diabetes and diabetes-related neuropathy. In the years 2010–2012, contracts with industry constituted an average of 13.5 % of third-party and project grants (cf. Appendix 3).

5. Staff development and promotion of junior researchers

Staff development and personnel structure

As of 31 December 2012, there were 194 members of staff (151.3 FTE) at DDZ, including 87 academic staff (69.3 FTE) and 20 Ph.D. students. Of the academic staff, the proportion of third-party financed personnel (FTE-based) was 41.9 % and the proportion of fixed-term positions was 79,3 % (cf. Appendix 4). There were 17 researchers at DDZ coming from abroad.

Promotion of gender equality

Overall, 60 % of DDZ's employees are female. As of 31 December 2012, the percentage of female researchers was 55 % at graduate and 55 % at postdoctoral/academic level (E13–E15). Amongst the scientists heading research units (i.e. research groups and institutes), three out of 15 were women (20 %). One female researcher was appointed to a professorship (W2-level) at Düsseldorf University Hospital (UKD) in 2010. None of the four institutes at DDZ or the Paul Langerhans Group is headed by a female scientist.

DDZ is committed to implementing the "Research-oriented Standards on Gender Equality" and the "Equality Implementation Agreement". Over the last few years, a working group, supported by the Equal Opportunities Officer, her deputy, and the Executive Board, has developed a catalogue of measures to reconcile work and family at DDZ. Based on this, DDZ successfully applied for the certificate of the "*audit berufundfamilie*" ("work & family audit"), which was granted in 2011.

On the basis of the **cascade model** ("*Kaskadenmodell*"), DDZ pursues the objective of achieving gender balance at all levels. Accordingly, DDZ agreed to continue the current gender quotas at W3- and W2-level (currently 0 % and 50 %, respectively) for the next five years up to 2017. In the same period, DDZ aims to raise the proportion of female scientists from currently 20 % to approx. 25 % at E15-level and from 36 % to 45 % at E14-level.

Promotion of junior researchers

DDZ supports the training of junior researchers from the beginning of their education onwards. Both Bachelor's and Master's theses in biology and biochemistry are offered at DDZ. Also, DDZ facilitates both Ph.D. and M.D. theses at the Faculty of Mathematics and Natural Sciences as well as the Medical Faculty at HHU Düsseldorf. Doctoral students are involved in one of three **structured programmes**: iGRAD (Interdisciplinary Graduate and Research Academy Düsseldorf), MedRSD (Medical Research School Düsseldorf) and VIVID ("in vivo investigations of metabolic pathomechanisms and diseases").

Between 2010 and 2012, a total of 20 doctoral degrees, 26 Master's and 28 Bachelor's degrees were completed at DDZ.

In 2009, DDZ established three **junior research groups**, all of which are headed by female scientists. Instruments for gaining qualifications and career development for junior scientists at DDZ include projects via Training and Feasibility Grants (TFG, cf. Chapter 6), exchange visits with collaborating partners, teaching opportunities and *Habilitation*, i.e. postdoctoral professorial qualification at HHU Düsseldorf.

In 2011, DDZ established two **Paul Langerhans Groups**, one of which was transformed into the Institute for Beta Cell Biology in 2013. Initially introduced for establishing new research topics, in the future, this instrument is scheduled to serve as a tool for developing excellent junior scientists and novel topics.

Vocational training for non-academic staff

Since 2012, DDZ has offered a training position for an apprentice animal keeper. Furthermore, DDZ plans to offer a training position for an office administrator from September 2013 onwards.

6. Quality assurance

Internal quality management

In 2001, DDZ implemented guidelines for safeguarding **good scientific practice**, addressing relevant issues of good scientific practice and internal quality management at different levels of its organisation. All clinical-experimental and epidemiological studies are performed according to the rules of good clinical practice or good epidemiological practice upon approval by the Human Ethics Board of Düsseldorf University Hospital (UKD) and are registered, if appropriate. All animal studies are approved by the responsible authority (*LANUV, Landesamt für Natur, Umwelt und Verbraucherschutz NRW*). For units involved in clinical studies, all staff members are required to take part regularly in external continuing education. Also, specific standard operating procedures ensure the standardised performance of laboratory and clinical procedures as well as data quality.

Quality management has been implemented for ongoing research projects by regular progress reports and discussions with the heads of research groups responsible for guideline compliance as well as within and across DDZ's subdivisions.

Since 2009, DDZ has initiated a step-wise process to establish the performance-based allocation of funds ("*Leistungsorientierte Mittelvergabe*", **LOM**). In 2010, the **Training and Feasibility Grant** system (TFG) was initiated as an in-house grant system, to which the institutes and the Paul Langerhans Group contribute approx. 9 % of their budget for consumables. The grant system aims to award funds (€ 120 k in 2012) to top-rated innovative interdisciplinary projects upon internal approval by the directors and by external review by the Scientific Advisory Board. Applications must be submitted jointly by at least two leading, non-group researchers from different units for one-year projects which employ a translational approach. So far, this has resulted in 25 joint abstracts as well as two papers and three external grant applications. Also, in 2012, the Board of Directors agreed on an **additional LOM concept** whereby one third of the overheads are returned to the grant-holding research group and the rest is used for common DDZ projects. On the level of the Institute for Clinical Diabetology, balanced, **performance-based funding allocation** was introduced in 2011 to distribute its budget for consumables.

Quality management by the Scientific Advisory Board and the Board of Trustees

The Scientific Advisory Board (SAB) and the Board of Trustees supervise quality management. SAB holds onsite meetings at least once annually. It advises DDZ on all scientific and strategic matters. The conclusions of the Scientific Advisory Board are submitted to the Board of Trustees and serve as the scientific expertise and basis for the decisions taken by the Board of Trustees and the General Assembly. To ensure short-term quality control, DDZ submits be-annual interim reports to SAB. DDZ also seeks

scientific approval by SAB for the programme budget it submits to the Federal and *Länder* Governments.

In accordance with DDZ's statutes, the Executive Board provides comprehensive information on all its activities and the chairman of SAB reports on his visits to DDZ during meetings with the Board of Trustees to form the basis for decisions.

Implementation of recommendations from the last external evaluation

The last onsite evaluation of DDZ took place in 2007. In its statement, the Senate of the Leibniz Association requested a report by the Scientific Advisory Board in which the SAB was asked to present its opinion on the implementation of the Senate's former recommendations. On the basis of that report, the Leibniz Senate issued a statement in 2009 including a number of recommendations (in *italics*) for the further development of DDZ. In order to meet these recommendations DDZ has implemented the following measures:

1) *"After the two previous appointment procedures for the leadership of the Institute for Clinical Biochemistry and Pathobiochemistry could not be completed successfully, a new recruitment procedure should be initiated at the earliest possible time with all relevant parties involved. With the help of a selection committee, attempts should be made to keep the period of the vacancy of this position as short as possible. The efforts that are made in this direction by the DDZ and the University of Düsseldorf to refill this position in the winter semester 2009/2010 are highly appreciated."*

According to DDZ, the Executive Board rapidly initiated another recruitment procedure resulting in the joint appointment of the current director of the Institute for Clinical Biochemistry and Pathobiochemistry with Heinrich Heine University Düsseldorf in March 2011.

2) *"The recruitment of junior research groups that have already been planned or planned to be established in the future are to be pursued with high priority."*

Since 2009, three junior research groups have been established at DDZ (cf. Chapter 5):

- Junior Research Group Health Services Research and Health Economics in 2009
- Junior Research Group Signal Transduction in 2009
- Junior Research Group Metabolic Imaging in 2010

3) *"A patient collective, which is currently being built, has to be a future focus of interaction of the institutes of the DDZ on the one hand and institutionalised collaborations on the other. Already in 2007 this has been recognised by the Senate as an essential unique characteristic of the DDZ. DDZ should exploit their opportunities much stronger than before. This includes clarifying the link between the research program and the collective."*

   "It should be ensured that DDZ keeps the leading management if the DDZ cohort continues as a multicenter study in the network of the German Center for Diabetes Research."

   "The cooperation of DDZ under the 2009 newly-founded German Center for Diabetes provides a way for intensification of future research and collaborations. In developing

these partnerships, DDZ must take care that the Center distinguishes itself through a coherent independent research program."

Originally planned as a monocentre study, DDZ launched the German Diabetes Study (GDS) comprising 636 patients on 31 December 2012. Since 2009, the GDS has also made a major contribution to the research programme of the German Center for Diabetes Research (*DZD e. V.*). On its own account, DDZ is not only the principal and coordinating study centre but also serves as the training centre for other study centres by offering expertise in the performance of clinical experimental modules. Between 2011 and 2012, DDZ finalised a concept and started integrating other groups for recruiting and studying patients. The GDS is currently being expanded by the addition of other modules, but DDZ continues to be responsible for scientific and organizational leadership and has recruited the vast majority of patients to date.

In order to exploit the potential of the study for the development of the research programme and intensify collaboration between the institutes, a steering committee of internal and external experts was formed. Also, the Clinical Research Center (CRC) was established to organise and conduct the clinical examination and logistics.

Under DDZ' research programme D, the Institute for Clinical Diabetology is responsible for clinical and clinical-experimental aspects, the Institute for Biometrics and Epidemiology for all aspects of data management analyses and the Institute for Biochemistry and Pathobiochemistry for sample processing, preparation and genomic data analysis. According to DDZ, various projects now form links between and across the research programmes and thus between all its subdivisions.

According to DDZ, its unique feature within the German Center for Diabetes Research (*DZD e. V.*) resides in a coherent strategy to study and follow up patients with overt diabetes and their complications. The uniqueness of DDZ's research programme is characterised by a transdisciplinary and translational concept to examine the mechanisms underlying the development of type 2 diabetes on molecular, clinical and epidemiological levels.

4) "To establish stable and long-term patient contacts and thus maintaining the clinical resources that are essential for the translational research, it is necessary to ensure a more secure and sustainable strengthening of the clinical department. The Senate appreciates the close cooperation of the DDZ with the Heinrich-Heine University and University Hospital Düsseldorf as well as the promises of both partners, which are important for the further development of the DDZ."

DDZ's scientific director was appointed as the director of the new Department of Metabolic Diseases at Düsseldorf University Hospital in 2009. The unit was continuously enlarged, starting with outpatient services and eight clinical beds for diabetes, diabetic foot syndrome, obesity and metabolic diseases. According to the original plans, the new director took over the previous chair of Endocrinology and Diabetology at HHU and directorship of the Department of Endocrinology and Diabetology at Düsseldorf University Hospital in 2012. At present, the infrastructure with a total of 21 clinical beds and additional outpatient services for general endocrinology including thyroid diseases and

diabetology provides optimal conditions for translational research and postgraduate training for clinical researchers. It also formed the basis for scientific collaboration with various university hospitals.

5) *"The proportion of temporary scientific posts should be increased."*

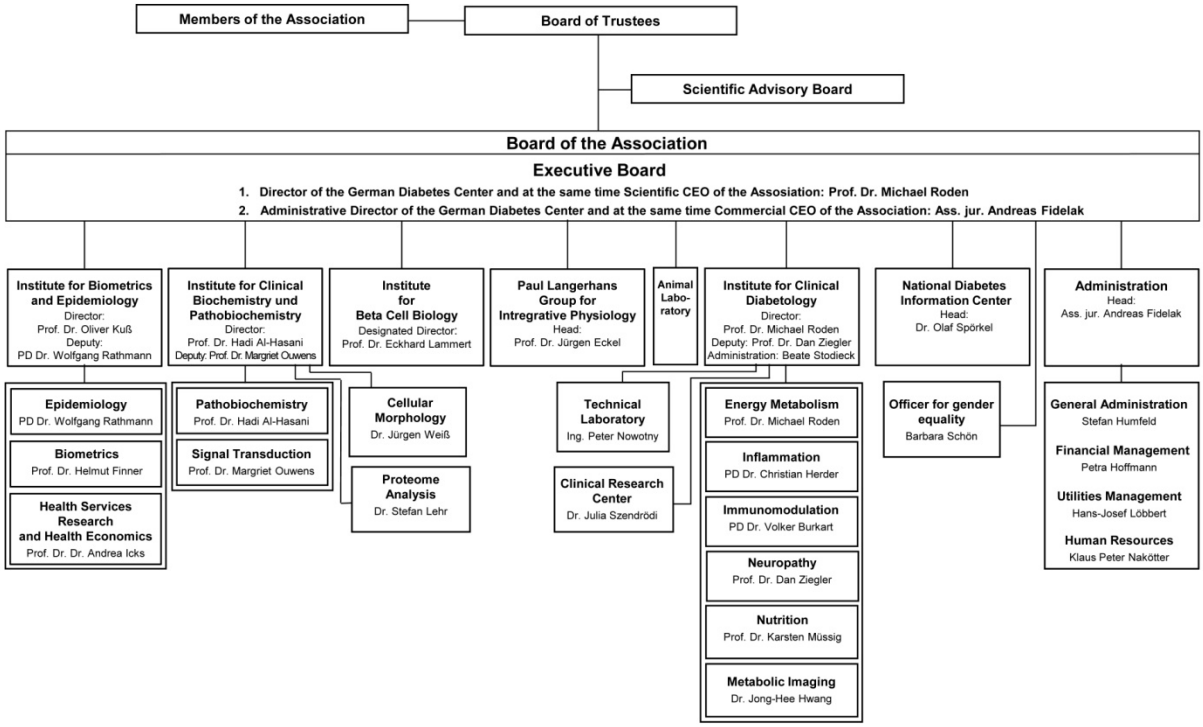
At the end of 2008, the proportion of permanent contracts amongst the institutionally financed scientific staff was 66 %. In 2012, this proportion had dropped to 39 %.

6) *"The Senate appreciates that the chair of the Scientific Advisory Board will be replaced shortly."*

The current chairman of the Scientific Advisory Board assumed office in October 2012.

Appendix 1

Organisational Chart



Responsibilities of the Institutes, PLG and Staff Units for the Research Programme

		Research Programmes			
		A: Identification of novel pathogenic mechanisms and molecular targets for diabetes mellitus	**B: Investigation of the development and sequelae of diabetes mellitus**	**C: Research on the epidemiological basis and models of diabetes prevention and care**	**D: Determination of the individual progression of diabetes mellitus in adulthood** (GDS study)
Institutes	Institute for Clinical Diabetology	+	+++	+	+++
	Institute for Clinical Biochemistry and Pathobiochemistry	+++	+	+	++
	Institute for Biometrics and Epidemiology	+	+	+++	++
	Institute for Beta Cell Biology	++ (A.2)	+		+
	PLG for Integrative Physiology	++ (A.3)	+		+
Staff Units	Animal Facility	++	+		
	National Diabetes Information Center	+	+	+	+

The Institutes and the Paul Langerhans Group (PLG) are responsible for the specific programmes. "+++": programme leader, "++": subprogramme leader, "+" collaborator; A.2: Pathophysiology of the beta cell; A.3: Endocrine and paracrine cell and organ crosstalk.

Appendix 2

Publications and patents

	Period		
	2010	**2011**	**2012**
Total number of publications	**137**	**157**	**175**
Original articles in peer-reviewed journals [1)]	59	79	90 (23)
Original articles from consortia in peer-reviewed journals [1)]	10	23	18 (3)
Review articles in peer-reviewed journals [1)]	22	21	16 (3)
Total number (originals incl. consortia, reviews) [1)]	**91**	**123**	**124 (29)**
Articles in other journals	17	10	28
Editorials, commentaries, case reports	19	18	13
Monographs	–	–	1
Editorship of edited volumes	1	–	2
Individual contributions to edited volumes	9	6	7
Number of publications per full-time equivalent (FTE) in 'research and scientific services' (not including doctoral candidates) [2)]	1.7	2.1	2.0 (0.5)

Industrial property rights (2010–2012) [3)]	Granted	Registered
Patents	–	3
Other industrial property rights	–	–
Exploitation rights/licences (number)	–	

[1] Contributions that have been accepted for publication but not yet appeared are added in parenthesis.
[2] The ratio "number of publications/FTE" was calculated on the basis of the number of original articles and original articles from consortia in peer-reviewed journals.
[3] For financial expenditures regarding revenues from patents, other industrial property rights and licences see Appendix 3.

Appendix 3

Revenue and Expenditure

Revenue		2010			2011			2012 [1]		
		k€	% [2]	% [3]	k€	% [2]	% [3]	k€	% [2]	% [3]
Total revenue (sum of I., II. and III.; excluding DFG fees)		**16.527**			**14.834**			**16.400**		
I.	**Revenue (sum of I.1., I.2. and I.3)**	**12.896**	**100,0**		**13.316**	**100,0**		**15.944**	**100,0**	
1.	Institutional funding (excluding construction projects and acquisition of property)	9.954	77,2		10.242	76,9		10.977	68,9	
1.1	Institutional funding (excluding construction projects and acquisition of property) by Federal and *Länder* Governments according to AV-WGL	9.954			10.117			10.977		
1.1.1	*Institutional funding received through the Leibniz competitive procedure (SAW-Verfahren)* [4]	459			389			239		
1.2	Funding of equipment (North Rhine-Westphalia)	–			125			–		
2.	Revenue from project grants	2.942	22,8	100,0	3.074	23,1	100,0	4.967	31,1	100,0
2.1	DFG	402		13,7	443		14,4	479		9,7
2.3	Federal, *Länder* Governments	642		21,8	778		25,3	653		13,1
2.4	EU	54		1,8	5		0,2	448		9,0
2.5	Industry	255		8,7	482		15,7	811		16,3
2.6	Foundations	389		13,2	166		5,4	491		9,9
2.7	Other sponsors (German Center for Diabetes Research – *DZD e. V.*)	1.200		40,8	1.200		39,0	2.085		42,0
3.	Revenue from services	–	–		–	–		–	–	
3.1	Revenue from commissioned work	–			–			–		
3.2	Revenue from publications	–			–			–		
3.3	Revenue from exploitation of intellectual property for which the institution holds industrial property rights (patents, utility models, etc.)	–			–			–		
3.4	Revenue from exploitation of intellectual property without industrial property rights	–			–			–		
3.5	*Revenue from other services, if applicable; please specify*	–			–			–		
II.	**Miscellaneous revenue** (*e.g.* membership fees, donations, rental income, funds drawn from reserves)	**252**			**231**			**456**		
III.	**Revenue for construction projects** (institutional funding by Federal and *Länder* Governments, EU structural funds, etc.)	**3.379**			**1.287**			–		

Expenditures		k€	k€	k€
Expenditures (excluding DFG fees)		**16.527**	**14.834**	**16.400**
1.	Personnel	7.111	7.811	8.149
2.	Material resources	4.675	4.985	6.224
2.1	Expenditures used for registering industrial property rights (patents, utility models, etc.)	33	26	31
3.	Equipment investments and acquisitions	1.332	1.061	1.632
4.	Construction projects, acquisition of property	3.235	1.450	–
5.	"Reserves" (*e.g.* cash assets, unused funds)	174	- 473	395
6.	Miscellaneous items	–	–	–

DFG fees (if paid for the institution – 2.5 % of revenue from institutional funding)	255	245	268

[1] Preliminary data: no
[2] Figures I.1, I.2 and I.3 add up to 100 %. The information requested here is thus the percentage of "Institutional funding (excluding construction projects and acquisition of property)" in relation to "Revenue from project grants" and "Revenue from services".
[3] Figures I.2.1 to I.2.7 add up to 100 %. The information requested here is thus the percentage of the various sources of "Revenue from project grants".

Appendix 4

Staff

(Basic financing and third-party funding / proportion of women (as of: 31 December 2012))

	Full time equivalents		Employees		Female employees	
	Total	thereof on third-party funding	Total	thereof on temporary contracts	Total	thereof on temporary contracts
	number	percent	number	percent	number	percent
Research and scientific services	**69.3**	**41,9**	**87**	**79,3**	**46**	**95,7**
Professors / Directors (C4, W3 or equivalent)[1]	3.0	–	3	100,0	–	–
Professors / Directors (C3, W2, A16 or equivalent)[2]	2.0	–	2	50,0	1	100,0
Adjunct Professors (E15)	3.0	16,7	4	25,0	–	–
Academic staff (E15)	5.5	9,1	6	66,7	2	100,0
Academic staff (E14)	21.0	38,1	24	54,2	10	80,0
Academic staff (E13)	23.2	50,5	28	96,4	22	100,0
Doctoral candidates (E13/2 or equiv.)	11.6	72,0	20	100,0	11	100,0
Service positions	**60.7**	**21,6**	**70**			
Laboratory (E9 to E12, upper-mid-level service)	19.6	5,1	21			
Laboratory (E5 to E8, mid-level service)	10.2	41,2	12			
Animal care (E5 to E8, mid-level service)	4.0	–	4			
Documentation/ other staff (E9 to E12, upper-mid-level service)	5.5	45,5	6			
Documentation/ other staff (E5 to E8, mid-level service)	7.0	21,1	8			
Clinical Research Center / Study Nurses or equiv. (E9 to E12, upper-mid-level service)	2.0	–	3			
Clinical Research Center / Study Nurses or equiv. (E5 to E8, upper-mid-level service)	9.4	41,7	13			
Technical service (E5 to E8, mid-level service)	3.0	–	3			
Administration	**16.0**	–	**17**			
Head of administration	1.0	–	1			
Staff positions (E9 to E12, upper-mid-level service)	4.0	–	4			
Internal administration (financial administration, personnel etc.) (E9 to E12, upper-mid-level service)	2.6	–	3			
Internal administration (financial administration, personnel etc.) (E5 to E8, mid-level service)	6.6	–	7			
Building service (E1 to E4)	1.8	–	2			
Student assistants	4.3	37,6	19			
Trainees	**1.0**	–	1			
Scholarship recipients at DDZ	**4.0**	100,0	**5**		**2**	
Doctoral candidates	1.0	100,0	2		–	
Post-doctoral researchers	3.0	100,0	3		2	

[1] All positions at W3-Level as well as one position at W2-level are financed directly by Heinrich Heine University Düsseldorf. These positions are not part of joint institutional funding by the Federation and the *Länder* (cf. Chapter 1).
[2] Including one position (1.0 FTE) of the head of the Technical Laboratory.

23 April 2014

Annex B: Evaluation Report

German Diabetes Center (DDZ), Leibniz Institute for Diabetes Research at Heinrich Heine University Düsseldorf

Contents

1. Summary and main recommendations

The work conducted at the German Diabetes Center, Leibniz Institute for Diabetes Research (DDZ) at Heinrich Heine University Düsseldorf, focuses on the prevention, early detection, diagnosis and therapy of *Diabetes mellitus* and its sequelae as well as on improving the availability of epidemiological data on its condition.

In the recent past, DDZ had experienced a decade of change and critical development during which, in particular, extended vacancies at the level of leading scientific personnel had meant it had not managed to initiate and appropriately implement necessary reforms.

Only when the position of Director was filled in 2008, was the centre able to embark on a successful realignment process both in terms of organisation and work focus. Since then, new appointments have been made to all the leadership positions in the institutes. DDZ has also managed to initiate crucial changes in work focus by developing the emphasis on translational research in its overall strategy. Now, work convincingly combines elements of fundamental research with clinical/experimental and epidemiological research as well as incorporating information for patients and health economic studies. Furthermore, by establishing new research groups and junior research groups DDZ has sparked a remarkable degree of dynamism in its work focus.

These changes have led to notable and extremely positive developments. Scientific productivity and the concomitant national and international visibility have been increased. The performance of DDZ's research groups is rated as "very good to excellent" in two cases, "very good" in two cases and "good to very good" in one case. As the Senate had recommended, the centre has very successfully addressed the issue of developing its patient collective, which now forms the basis for both internal and a number of external collaborations, for example at the German Center for Diabetes Research (DZD). DDZ has also managed to significantly enhance its cooperation with Heinrich Heine University (HHU) and Düsseldorf University Hospital in the fields of research and teaching, graduate supervision, and inpatient care. It has improved its publication performance and the volume of funding acquired for research.

The restructuring, which was launched successfully in the last few years, has, however, not yet been completed. In order to consolidate positive developments and sustain visibility the centre must, therefore, perpetuate its commitment to driving the ongoing processes of change.

Special consideration should be given to the following main recommendations in the evaluation report (highlighted in **bold face** in the text):

1. Overall, DDZ has developed remarkably and extremely positively in the last few years. The processes of change that have been initiated now provide the foundations for continuing the successful development of the Diabetes Center, where topics are addressed using an overarching, interdisciplinary approach. DDZ's leadership must continue its commitment to driving these processes which have not yet all been completed due to the fact that the leadership positions were only filled in the recent past.

2. DDZ's past performance has generated substantial and necessary progress which it should now use to enhance its scientific visibility yet further. To achieve this, the working units that produced fewer publications in the past or were less successful in acquiring competitive funding, must also play a more active role in the future.
3. DDZ should remember that it is still in the throes of transition. The personnel restructuring of the institutes has, admittedly, largely been completed and, once the work focus had been successfully realigned, scientific productivity increased in subsequent years and collaboration not only within the centre but also with external partners was improved further. The consolidation in personnel and structures must, however, be perpetuated in content terms as well. This will enable DDZ to reinforce its position as a national reference centre for clinical diabetes research tasked with providing information and advice to the general public and to become more visible both in Germany and internationally.
4. It is recommended to continue diversifying the portfolio of third-party funding and, in particular, to increase the amount of funding acquired from the EU and the DFG.
5. The Review Board endorses DDZ's plans to purchase a high-field veterinary MRT scanner. This purchase is necessary, for example, in order to conduct in vivo measurements of glycogen and ATP synthesis rates in mouse models and compare them with clinical studies on humans.
6. The Review Board considers the National Diabetes Information Center to be an exceptionally important component of DDZ that is of strategic significance for its position as a non-university national reference centre for diabetes research. Information provision is also very important because it helps to prevent the disease. However, the provision of staff and resources as well as the scope of the centre are not yet in accordance with its strategic significance. It is therefore recommended to strengthen the National Diabetes Information Center sustainably by research activities in the social science and health education sectors and to increase its visibility significantly amongst academics, doctors and patients. In order to achieve these goals, the information centre's financial provisions must be enhanced also by DDZ's own funding, strategic research collaborations must be organised and web-based social networks must be utilised to a greater extent than has been the case so far.
7. In the past, DDZ has tried to increase the proportion of women researchers who also hold positions of responsibility. However, the current proportion of women amongst the leading scientific personnel is clearly too low. DDZ is expected to implement the agreed target quotas contained in the binding cascade model. For this purpose, it is necessary to keep intensifying, amongst others, efforts to recruit excellent, female (junior) researchers internationally.
8. According to the statutes, the Chair of DDZ's Scientific Advisory Board is a voting member of the Supervisory Board. In order to make a clear distinction between the functions of supervision and scientific advice, this regulation must be changed. As is usually the case at Leibniz institutions, the Chair of the Scientific Advisory Board

should be a non-voting member of the Supervisory Board in a purely advisory capacity.

9. Attention is drawn to the fact that the management principles (*Bewirtschaftungsgrundsätze*) currently in place at DDZ do not conform to the valid resolutions on the implementation of the *Ausführungsvereinbarung WGL*. They must be adjusted as soon as possible.

2. General concept and profile

The German Diabetes Centre (DDZ) focuses on the prevention, early detection, diagnosis and therapy of *Diabetes mellitus* and its sequelae as well as on improving the availability of epidemiological data on its condition. Against the backdrop of growing prevalence worldwide, DDZ pursues the overarching goal of employing interdisciplinary research approaches to reduce the burden on the individual and society that results from *Diabetes mellitus.*

The centre is divided into four institutes, a Paul Langerhans Group and two staff units, which for the purposes of the evaluation were presented as working units within the centre. Within these sub-units there are eleven research groups and junior research groups as well as four laboratory and service units at DDZ.

Development of the institution since the last evaluation

In the previous ten years, the institute had gone through a very critical phase. Due, in particular, to changes in personnel and subsequent extended vacancies at the leadership level of both the centre and the institutes, DDZ had not managed to initiate and implement the necessary reforms appropriately. As a result, in the external evaluations of 2003 and 2007, the Diabetes Center had received a critical assessment. The statement by the Leibniz Senate of November 2009 on a report by DDZ's Scientific Advisory Board on implementing recommendations had also come to the conclusion that DDZ must continue to drive the implementation of its recommendations on work focus and structure.

The centre received the major impetus required to launch the reforms demanded by the Senate when the position of DDZ Director was filled in August 2008. Essentially under his leadership the process of organisational, structural and scientific realignment was started, actively supported not only by the committees and funders but also by the staff at the centre. Overall, DDZ has made significant and very positive progress since the last evaluation, especially in comparison with the situation in 2007.

Apart from the successful recruitment of the Director, who assumed his position in combination with the leadership of the Institute for Clinical Diabetology in 2008, in 2011, after considerable delays, it was also possible to fill the position of head of the Institute for Clinical Biochemistry and Pathobiochemistry, which had been vacant since 2006. Finally, in October 2013, immediately prior to the evaluation visit, the head of the Institute for Biometrics and Epidemiology was appointed jointly with Heinrich Heine University Düsseldorf. The previous head had retired shortly beforehand. In 2011, DDZ established two so-called Paul Langerhans Groups. One of the heads of these groups was an external,

the other an internal appointment. In July 2013, one of these two groups became the fourth DDZ institute, the Institute for Beta Cell Biology. Furthermore, in 2009, DDZ set up three junior research groups, one of which has since become a regular DDZ research group.

In parallel, the centre restructured its laboratory and infrastructure sectors by transforming its existing scientific infrastructure, which had been extended since the previous evaluation, into four so-called Staff Units in 2011 and assigning them to two DDZ institutes for organisational purposes. In addition, since 2009, DDZ has been operating a National Diabetes Information Center.

Against this backdrop, DDZ has successfully implemented the overall strategy that received a positive response at the last evaluation in 2007. In particular, yet greater emphasis has been placed on translational research approaches which now form a very convincing, integral part of the research portfolio. This has been helped by highly successful collaboration between DDZ and Düsseldorf University Hospital, which was placed on a new footing in 2007, thus facilitating the linkage of sustainable inpatient care and clinical/experimental research – as recommended by the Leibniz Association Senate.

The centre now has a coherent research strategy involving four, closely interlinked programmes. The cross-cutting themes that are addressed jointly by the institutes are both innovative and in line with the current state of research. In this context, DDZ's working units now focus convincingly on linking elements of fundamental research with clinical/experimental research questions. Some of the work is already bridging the gap between model and patient quite remarkably, whereby the approach applied to the topics by DDZ's institutes and research groups is overarching and employs complex methods and a long-term perspective that can only properly be realised at a non-university research institution. In the opinion of the Review Board, the realignment of the research focus that has been stepped-up by the leading scientists appointed since 2008 has made an outstanding contribution to driving DDZ's successful profiling.

Overall, DDZ has developed remarkably and extremely positively in the last few years. The processes of change that have been initiated now provide the foundations for continuing the successful development of the Diabetes Center, where topics are addressed using an overarching, interdisciplinary approach. DDZ's leadership must continue its commitment to driving these processes which have not yet all been completed due to the fact that the leadership positions were only filled in the recent past.

The Diabetes Center is divided up into institutes which themselves are split into research groups and junior research groups. In addition to establishing three junior research groups, in 2010, DDZ decided to set up two so-called Paul Langerhans Groups. The aim was to integrate important thematic additions into the structure of the centre with a view to establishing them permanently. Furthermore, since the last evaluation, the centre has introduced various tools for the allocation of performance-based funding in order to manage its own development more effectively.

It is welcomed that DDZ has created enough flexibility at the level of the various working units to allow them to address important topic areas at relatively short notice and to steer the scientific productivity in the individual units more efficiently. As a tool in this context, the Paul Langerhans Group has proved its worth and, in 2013, already led to the establishment of a fourth institute focussing on beta cell biology, which is of importance to DDZ in general. Furthermore, a group dealing with health services research and health economics, which was headed with considerable success by a junior researcher, was transformed into a permanent research group at DDZ. It is, therefore, only logical that DDZ is planning to establish additional groups and to utilise them to promote junior researchers to a greater extent than was previously the case. In the future, DDZ should use the existing performance-based funding tools, which have been tested in some areas, across the centre.

Results

The performance of the four institutes and the Paul Langerhans Group are rated as "very good to excellent in two cases, "very good" in two cases and "good to very good" in one case.

From 2010 to 2012, members of staff produced a total of 137, 157 and 175 publications per respective year, mostly in the form of original or review articles in reviewed journals. DDZ has thus managed to increase its publication output significantly in the last few years despite the initial vacancies and changes in personnel. In certain fields like energy metabolism or phenotyping in patients, DDZ's international visibility has increased noticeably. **DDZ's past performance has generated substantial and necessary progress which it should now use to enhance its scientific visibility yet further. To achieve this, the working units that produced fewer publications in the past or were less successful in acquiring competitive funding, must also play a more active role in the future.** The research groups and junior research groups are addressing numerous promising, innovative themes which should lead to growth in the number of publications.

In the last few years, DDZ has successfully developed and maintained existing cohorts and its patient collective. It managed significantly to increase the number of recruits participating, for example, in the German Diabetes Study (GDS), which is fundamental to the centre. In accordance with Senate expectations, the cohorts are now a convincing crystallisation point in cooperation between the institutes at DDZ, for example in the field of biomarker and phenotyping research. Furthermore, the GDS patient collective, headed by DDZ, is an essential basis for collaboration between DDZ and external partners at the German Center for Diabetes Research (DZD).

On the strength of the model project "development of an information and advisory service on *Diabetes mellitus*", funded by the Federal Ministry of Health from 2008 to 2013, DDZ provides useful, patient-oriented online services and information platforms for the public. Since these services were established, the website of the National Diabetes Information Center has been accessed more frequently with every successive year. In the light of this achievement, it is convincing that the centre is underlining its claim to be-

coming the national reference centre for clinical diabetes research tasked with providing information and advice to the general public (see also Chapter 3: National Diabetes Information Center).

Strategic work planning for the next few years

DDZ aims to continue generating knowledge on the mechanisms and factors determining the development and course of the disease *Diabetes mellitus* and its sequelae. For this purpose, it is planning to set up at least two additional junior research groups and continue increasing the number of participants in the existing cohorts, especially in the German Diabetes Study (GDS). The cohorts are an essential precondition for long-term research projects, which cannot be conducted in this way at a university. The centre would also like to extend its activities in large, multi-centre studies.

The milestones drafted by the centre are ambitious and clearly build on its strengths. They are due to be implemented in the context of the four programmes. For this purpose, DDZ leadership should utilise the managerial tools at its disposal especially as, in the past, they sparked a remarkable degree of dynamism and flexibility at the level of research groups and junior research groups**. At the same time, however, DDZ should remember that it is still in the throes of transition. The personnel restructuring of the institutes has, admittedly, largely been completed and, once the work focus had been successfully realigned, scientific productivity increased in subsequent years and collaboration not only within the centre but also with external partners was improved further. The consolidation in personnel and structures must, however, be perpetuated in content terms as well. This will enable DDZ to reinforce its position as a national reference centre for clinical diabetes research tasked with providing information and advice to the general public and to become more visible both in Germany and internationally.**

Appropriateness of facilities, equipment and staffing

The provision of institutional funding is adequate for DDZ to fulfil its statutory mission.

Since the last evaluation, DDZ has increased the amount of third-party funding it acquired from approx. one million EUR in 2007 to almost five million EUR in 2012. The proportion of project funding in terms of DDZ's overall budget increased from 10.5 percent in 2007 to 31 percent in 2012. DDZ has thus reached a very good level which should be maintained in the future. DDZ raised more than half of this funding through the Federation and the *Länder*, partly by its involvement in the German Center for Diabetes Research (DZD), which has brought the centre significant project funding since 2009. **It is recommended to continue diversifying the portfolio of third-party funding and, in particular, to increase the amount of funding acquired from the EU and the DFG.** New models of collaboration between DDZ and the pharmaceutical industry could be explored.

In the last few years, DDZ has managed to expand its technical infrastructure remarkably. The centre now has impressive facilities in the laboratory, animal and clini-

cal/experimental sectors. In this context it received very good support from the funder, especially with regard to necessary construction and refurbishment measures.

The Review Board endorses DDZ's plans to purchase a high-field animal MRT scanner. This purchase is necessary, for example, in order to conduct *in vivo* measurements of glycogen and ATP synthesis rates in mouse models and compare them with clinical studies on humans. In combination with the existing human scanner, the Review Board has identified major potential for future translational research on *Diabetes mellitus*.

3. Subdivisions of DDZ

Institute for Clinical Diabetology (32.8 FTE, thereof 11.0 FTE research and scientific services and 17.4 FTE service staff)

The Institute for Clinical Diabetology investigates the mechanisms underlying type 1 and type 2 diabetes as well as their sequelae. Six research groups, including one junior research group established in 2009, examine energy metabolism, inflammation processes, nutrition issues and neuropathological complications. The Clinical Research Center and the Technical Laboratory are assigned to the institute, which developed from the defunct *Deutsche Diabetes Klinik* in 2007/08.

In 2008, the current head assumed the position in addition to becoming Director of DDZ. Since then, the institute has undergone convincing realignment with regard to both contents and structure. It now has a great impact and stands out internationally.

The institute excels in connecting fundamental and clinical research and, based on this, also in therapeutic approaches. The transdisciplinary aspects of its work are impressive. The studies on liver metabolism in mouse models and the translation of research results to humans, in particular, are very remarkable. The work presented by the institute on the impact of congenital immunity on energy homeostasis, on sub-clinical infection, anti-inflammatory cytokines and neuropathic disorders is also convincing.

The institute has an impressively high level of technical facilities, including imaging systems. With the concomitant development of non-invasive procedures for measuring glucose and energy metabolism in various cell and tissue types it works at the very forefront of international research. The institute's plans to extend its technical infrastructure by purchasing a small animal high-field MRT scanner are meaningful and are expressly endorsed (see Chapter 2).

Overall, the institute's productivity has improved noticeably by comparison with 2007. The publication performance of staff in all working groups is rated as very good with great scientific impact. The institute has already made a name for itself internationally with its published research results, particularly those on deteriorated energy metabolism and patient phenotyping. In future, especially the groups that have produced fewer publications in the recent past should increase their output.

In the last few years, the institute has managed to keep increasing the volume of third-party project funding and, not least due to the funding for DZD e.V. has now reached a

very good level. Cooperation between research groups as well as with other institutes at DDZ and Düsseldorf University Hospital is remarkable.

The overall performance of the institute is "very good to excellent".

Institute for Clinical Biochemistry and Pathobiochemistry (27.4 FTE, thereof 11.5 FTE research and scientific services and 12.4 FTE service staff)

The Institute for Clinical Biochemistry and Pathobiochemistry investigates the molecular basis for the onset and progression of obesity, insulin resistance and type 2 diabetes, in particular the identification and molecular analysis of adipocyte-derived factors. The institute consists of the Pathobiochemistry Research Group under the head of the institute and a junior research group on Signal Transduction, founded in 2009. The Cellular Morphology and Proteome Analysis service platforms are assigned to the institute.

The current head assumed the position in March 2011, following a period of five years during which the present head of the Paul Langerhans Group for Integrative Physiology temporarily headed the institute. The developments that have taken place since 2011, particularly in the field of animal models and experimental mouse genetics as well as in expanding technical installations and equipment, are impressive and have been undertaken convincingly. This has opened up manifold methodological approaches which the institute utilises for its own benefit as well as for that of other research groups, which has generated interesting translational perspectives. With its outstanding, only recently established mouse models and existing methods of cell and molecular biological analysis the institute plays an exceptionally important, central role within DDZ, and as a collaborative partner outside.

The research conducted in the last two years is very promising – a poster presentation covered investigations on TBC1D family proteins, a study on the long-term effects of chronic stress and fat intake, an analysis of metabolomic profiles or biomarkers in connection with the German Diabetes Study (GDS) and work on the impact of epicardinal fat tissue on heart function. The research is rated as very good; in some cases it has the potential to be excellent. This is particularly true of the recently launched physiological investigations on the interplay between muscle and fat tissue. Plans for future investigations follow up convincingly.

The level of the publications produced by the institute so far is rated as good to very good. Staff have also been able to raise project funds in the last few years. In both areas, however, the Review Board does see (in some cases considerable) room for improvement.

The overall performance of the institute is "very good".

Institute for Biometrics and Epidemiology (31.2 FTE, thereof 19.5 FTE research and scientific services and 8.4 FTE service staff)

The Institute for Biometrics and Epidemiology investigates epidemiological questions and issues related to the prevention and care of *Diabetes mellitus* on the basis of population-based studies. The institute is divided up into three research groups. When the for-

mer head retired in October 2013, the position was taken on by a scientist appointed jointly with Heinrich Heine University Düsseldorf.

In the past, the research group on biometrics has produced good to very good work in biomathematics, which included important service tasks for the other DDZ research groups. Essentially, the work consisted of highly-specialised investigations which in future, however, should be more closely linked with existing cohort data, in the context of metadata analyses, for example. Similarly, translational aspects, which are central to DDZ's work as a whole, are not considered appropriately in the group's work. These aspects should be promoted and lead to a growth in the institute's productivity, not least to intensify cooperation with other groups inside and outside of DDZ going beyond the existing service tasks.

The research on public health and health economics is very impressive. The research group, which was launched as a junior research group in 2010, employs many innovative approaches. A particular emphasis is placed on transfer aspects, for example by considering other (widespread) diseases and not just issues related to *Diabetes mellitus.* The group is encouraged to place even greater emphasis on the comparative approach and to make use, amongst others, of the cohorts in which DDZ is involved, for example in the context of the European Diabetic Foot Study, as is intended. With its convincing publications, the group has generally achieved international visibility. It maintains many collaborative relations and reached an impressive level of third-party funding in a relatively short time. It is well on the way to becoming an excellent group in a field that has not been addressed sufficiently so far. In order to promote this process, DDZ should improve the research group's resources.

A third research group deals with basic issues of epidemiology in *Diabetes mellitus*, and its members have gained broad visibility within the discipline. The group is involved in numerous epidemiological platforms and has also managed to increase its publication performance and third-party funding considerably in the past. It has, in particular, managed to increase the publication figures for original articles. Based on its previous work, this group, like the biometric research group, should make greater use of the cohort data available at DDZ and utilise it for international comparative data analyses. By taking greater account of translational issues, which are of importance to the centre, the group should become better integrated in DDZ and develop further external collaborative relations.

Due to the change in leadership, at the time of the evaluation, the institute was in a transition phase. In the opinion of the Review Board, one significant future challenge will be to tap the data that is available at DDZ more effectively for their own purposes whilst creating the basis for greater collaboration with external partners at home and abroad. In general, both the biometric and the epidemiological research groups are called upon to develop and extend their research approaches and methodological perspectives further by drawing on this data.

In summary, the performance of the institute is rated "good to very good".

Institute for Beta Cell Biology (2.0 FTE, thereof 2.0 FTE research and scientific services)

The Institute for Beta Cell Biology was only created in July 2013 on the basis of the existing Paul Langerhans Group of the same name. DDZ's decision to consolidate the field of beta cell research by establishing the institute is understandable and is welcomed. DDZ is thus addressing an extremely relevant scientific field that links up ideally with the work conducted by DDZ's institutes and research groups. It also allows the centre to intensify cooperation with Heinrich Heine University Düsseldorf, and particularly with the Faculty of Mathematics and Natural Sciences, where the head of the institute holds a professorship.

The Institute for Beta Cell Biology investigates pancreatic beta cells. The group, comprising the head of the institute and an additional member of scientific staff, thus specifically focuses on an area of significant scientific interest which has generated outstanding publications since it was established as a working unit in 2012. The current work on NMDA receptors in beta cells is excellent. This is also true of the work on vascularisation as well as the translational approaches the group adopts in general. The volume of third-party funding acquired by the head of the institute is impressive.

The Review Board considers the small group to have considerable potential to produce very good to excellent results and the relevant outstanding publications. The plans presented by the head of the institute for future activities are convincing as is the amount of funding foreseen by DDZ to continue expanding the institute.

The overall performance of the institute is "very good to excellent".

Paul Langerhans Group for Integrative Physiology (9.1 FTE, thereof 3.8 FTE research and scientific services and 1.8 service staff)

The approaches chosen by the Paul Langerhans Group for their work on integrative physiology are of great significance to DDZ. The studies presented on novel adipokines and myokines are impressive, particularly for their convincing use of translational approaches. These allow the group to combine fundamental research with clinical practice and applications in an exemplary fashion. In its work the group utilises an impressive technical diversity.

The publication performance and volume of third-party project funding have reached a good to very good level, although the Review Board does identify growth potential, especially with regard to publications.

The Paul Langerhans Group for Integrative Physiology was established in 2011. As of 2006, the current head had been the acting head of the Institute for Clinical Biochemistry and Pathobiochemistry. As he will be retiring in 2014, DDZ should ensure that the group's work, which is fundamental to the centre as a whole, is continued in an appropriate form.

The overall performance of the institute is "very good".

National Diabetes Information Center (5.0 FTE, thereof 2.5 FTE research and scientific services and 2.5 FTE service staff)

In the shape of the National Diabetes Information Center, which was established in 2009, DDZ has an important tool at its disposal for transferring recent research results to the public and for providing patients with scientifically-sound information. It is welcomed that DDZ intends to continue developing the information centre that was established on the basis of funding provided by the Federal Ministry of Health (BMG) for the period 2008 to 2013. An important step, which has been planned in this context, is to employ utilisation studies to systematically extend and optimise the portfolio and enhance the user friendliness of the information presentation.

The Review Board considers the National Diabetes Information Center to be an exceptionally important component of DDZ that is of strategic significance for its position as a non-university national reference centre for diabetes research. Information provision is also very important because it helps to prevent the disease. However, the provision of staff and resources as well as the scope of the centre are not yet in accordance with its strategic significance. It is therefore recommended to strengthen the National Diabetes Information Center sustainably by research activities in the social science and health education sectors and to increase its visibility significantly amongst academics, doctors and patients. In order to achieve these goals, the information centre's financial provisions must be enhanced also by DDZ's own funding, strategic research collaborations must be organised and web-based social networks must be utilised to a greater extent than has been the case so far.

Animal facilities (5.0 FTE, thereof 1.0 FTE research and scientific services and 4.0 FTE service staff)

DDZ has very well equipped animal, specifically mouse, facilities. The restructuring, investment and equipment additions that have taken place since 2011 have proved their worth. The section is extremely well organised and manages its resources and costs efficiently. It has impressive expertise and employs a broad range of technology, for example for breeding its own mouse lines or for the phenotyping of mouse models. The staff ensure that the treatment and care of the mice are excellent. On this basis, a remarkably large range of scientifically highly interesting animal models are developed.

DDZ's plans to improve the technical equipment at the centre by purchasing a small animal high-field MRT scanner are expressly endorsed and should be implemented (see Chapter 2).

4. Collaboration and networking

Collaboration with universities

At the time of the evaluation visit, four leading scientists, including the Director, were W-3 or W-2 professors at the Faculty of Medicine or the Faculty of Mathematics and Natural Sciences at **Heinrich Heine University Düsseldorf** (HHU). The choice of incumbents was made jointly. The positions are financed entirely by HHU. Another joint

appointment of a leading scientist, made in October 2013, is being financed from DDZ funding (Jülich Model). Furthermore, four scientists financed by DDZ also held associate professorships at HHU Düsseldorf.

It is welcomed that DDZ and the university cooperate successfully in the field of research and teaching as well as in the joint supervision of graduates. DDZ coordinates the future focus areas "Diabetes" and "Health and Society" at HHU. Regulations allowing DDZ's scientific staff to conduct their own, patient-oriented, clinical/experimental research at Düsseldorf University Hospital (with concomitant reductions in the work load at DDZ) have proved their worth and are welcomed. Overall, collaboration has developed very well.

Collaboration with **Düsseldorf University Hospital** (UKD) has developed extremely well indeed. After the closure of the *Deutsche Diabetes-Klinik* and the outsourcing of medical/clinical work from DDZ in 2007, as early as 2008, the centre managed to open a clinical department with 12 beds at UKD. As a result of appointing the Director of DDZ as the head of the Department of Endocrinology and Diabetology at UKD in 2013 and the amalgamation of the clinical units, the number of beds increased to 21. As recommended by the Senate in 2007, access to inpatient care and clinical resources, which are essential for DDZ, was thus placed on a long-term, permanent and secure footing.

Collaboration with other domestic and international institutions

Since 2009, DDZ has cooperated with four other university and non-university diabetes research institutions in the framework of the German Center for Diabetes Research (**DZD** e. V.), a German Centre for Health Research. Cooperation is close and generates great scientific and financial added-value for DDZ. Another positive aspect is that DDZ has managed to assume a leading role within DZD and, in particular, to make its mark in the German Diabetes Study, despite the internal restructuring and manifold changes.

Recently, DDZ has become involved in the **National Cohort**, a multi-centre, long-term population study. This involvement is welcomed; it should, however, not be pursued at the expense of the existing cohorts and patient collective at DDZ. The funders are expected to provide adequate financing for DDZ's involvement in the National Cohort.

DDZ is successfully involved in a wide range of national and international networks. Special mention should be given to its particular commitment to the European Association for the Study of Diabetes (EASD). It has also been able to extend its collaboration with (non-)university partners abroad. Within the **Leibniz Association** it is actively involved in the Leibniz Research Alliance on Healthy Ageing.

In the framework of small-scale studies and test series, it is scientifically fruitful for DDZ to cooperate with partners in the pharmaceutical **industry**, who themselves have a focus on fundamental research into *Diabetes mellitus.* The requisite internal funding provided by DDZ is used purposefully and should continue to be provided in the future, too. As the translational research jointly with the industry has still growth potential, opportunities for intensifying such collaborations should not be overlooked and, in the course of consolidating the centre, should be fostered in the mid-term.

5. Staff development and promotion of junior researchers

Staff development and personnel structure

Since the last evaluation in 2007, new appointments have been made to all the leadership positions in the institutes. In August 2008, the current Director assumed office. He has energetically implemented the recommendations from the last evaluation and steered the centre into an internationally competitive position.

In the following years, a total of five new research and junior research groups were set up. The number of staff grew accordingly from 141 in 2008 to approx. 200 (as of 31.12.2012). At the same time, in accordance with a Senate recommendation, the proportion of permanent staff on institutionally-funded positions in research and scientific services dropped to approx. 40 % (2008: 66 %). With its current personnel figures the centre is able to address its selected themes efficiently and comprehensively.

Promotion of gender equality

DDZ's four institutes and the Paul Langerhans Group are headed by scientists. On the reporting date (31.12.2012) at research group level, three of the junior research groups set up in 2009 and 2010 were headed by women researchers; of these, one woman researcher was appointed to a W-2 professorship in the Faculty of Medicine at HHU in 2010; a further female junior research group leader left the centre in 2013. The Clinical Study Center is also headed by a female scientist.

In the past, DDZ has tried to increase the proportion of women researchers who also hold positions of responsibility. At 13 percent, however, the current proportion of women amongst the leading scientific personnel (E15 and higher) is clearly too low. DDZ is expected to implement the agreed target quotas contained in the binding cascade model. For this purpose, it is necessary to keep intensifying, amongst others, efforts to recruit excellent, female (junior) researchers internationally.

In 2011, DDZ was awarded the *audit berufundfamilie* certificate. A variety of measures has been introduced to reconcile work and family which provide good support for members of staff.

Promotion of junior researchers

Since the last evaluation in 2007, DDZ has significantly increased its collaboration with HHU in the field of graduate promotion. Currently, doctoral candidates take part in three different graduate programmes at Heinrich Heine University. A further positive aspect is that DDZ not only supervises doctoral candidates in medicine but also in the natural sciences. All in all, the situation has improved since 2007 both in terms of quality and quantity. On 31.12.2012, 20 doctoral candidates were being supervised by scientific staff at the centre. Plans to enhance the supervision of doctoral candidates by developing a central contact point are welcomed.

In accordance with the recommendations from the last evaluations, in 2009 and 2010, three very successful junior research groups were established. In doing so, DDZ suc-

ceeded in sparking important dynamism at the centre. The Review Board endorses DDZ's plans for setting-up additional junior research groups and recommends it to make efforts to acquire the requisite third-party funding.

It is welcomed that DDZ is involved in specialist training for doctors and that it defines this as an element of promoting junior physicians.

Vocational training for non-academic staff

Currently, DDZ offers one position for an apprentice animal keeper and one for a trainee in office administration. It is welcomed that DDZ would like to increase the number of trainees at the centre and intends to introduce a further four positions for trainees.

6. Quality Assurance

Internal quality management

Quality management is transparent and conforms to the usual standards at Leibniz institutions. The administration is very well organised and equipped. The change of administrative leadership in 2013 went smoothly.

Since 2009, DDZ has been operating performance-based funding allocation (LOM), the main feature of which are so-called Training Feasibility Grants. They have proved their worth as they allow DDZ to promote collaboration between the working units, and facilitate innovative projects on the basis of competitively awarded grants. Junior researchers, in particular, benefit from this tool. DDZ's plans to extend performance-based funding allocation to embrace consumables was tested in a pilot phase and proved promising.

Quality management by the Scientific Advisory Board and Board of Trustees

The Scientific Advisory Board (SAB) carries out its duties conscientiously and attentively. In the last few years, it supervised and supported DDZ through a period of extremely difficult and critical upheaval with great diligence. As was the case in 2012, the SAB should continue to monitor the centre on the level of research groups and junior research groups.

It is welcomed that, since 2012, the function of Chair of the Board no longer falls to the representative of one of DZD's collaborative partners, thus implementing a recommendation made by the Leibniz Senate in 2009 to avoid conflicts of interest.

According to the statutes, the Chair of DDZ's Scientific Advisory Board is a voting member of the Supervisory Board. In order to make a clear distinction between the functions of supervision and scientific advice, this regulation must be changed. As is usually the case at Leibniz institutions, the Chair of the Scientific Advisory Board should be a non-voting member of the Supervisory Board in a purely advisory capacity.

In the future, the members of the SAB should be elected by the Supervisory Board (and not just after a hearing) for a maximum period of four years (and not six as at present). Re-election should only be allowed once.

Attention is drawn to the fact that the management principles (*Bewirtschaftsgrundsätze*) currently in place at DDZ do not conform to the valid resolutions on the implementation of the *Ausführungsvereinbarung WGL*[1]. They must be adjusted as soon as possible.

Implementation of recommendations from the last external evaluation

In the opinion of the Review Board, DDZ implemented the recommendations made by the Senate of the Leibniz Association in 2009 in their entirety. These recommendations referred to (see also Status Report, p. A-19f):

(1) appointing a new head of the Institute for Clinical Biochemistry and Pathobiochemistry (see Chapters 2 and 3)

(2) establishing junior research groups (see Chapters 2 and 5)

(3) extending and developing DDZ's own patient collective (see Chapters 2 and 3)

(4) securing permanent access to inpatient care and clinical resources (see Chapter 4)

(5) increasing the proportion of fixed-term positions (see Chapter 6)

(6) changing the function of the Chair of DDZ's Scientific Advisory Board (see Chapter 6)

[1] Administrative Agreement between the Federal and *Länder* Governments with regard to the joint funding of member institutions of the Leibniz Association.

Appendix

1. Review Board

Chair (Member of the Leibniz Senate Evaluation Committee)

Gisa **Tiegs**	Institute of Experimental Immunology and Hepatology, University Medical Center Hamburg-Eppendorf, Germany

Deputy Chair (Member of the Leibniz Senate Evaluation Committee)

Hans **Spada**	Institute of Psychology, University of Freiburg, Germany

Reviewers

Bernhard **Brüne**	Institute of Biochemistry I, Faculty of Medicine, Goethe University Frankfurt, Germany
Emanuelle **Canet-Soulas**	Research Laboratory in Cardiovascular, Metabolism, Diabetologia and Nutrition (CarMeN, INSERM U 1060), University Lyon 1, France
Mary **Cotter**	Department of Biomedical Sciences, University of Aberdeen, United Kingdom
Meredith **Hawkins**	Diabetes Research Center, Albert Einstein College of Medicine, New York, USA
Anne **Jörns**	Institute of Clinical Biochemistry, Hannover Medical School, Germany
Roy **Taylor**	Magnetic Resonance Centre, Newcastle University, United Kingdom
Karl **Wegscheider**	Department of Medical Biometry and Epidemiology, University Medical Center Hamburg-Eppendorf, Germany

Representative of the Federal Government

Ingo **Höllein**	Federal Ministry of Education and Research, Bonn, Germany

Representative of the Länder *Governments (Member of the Leibniz Senate Evaluation Committee)*

Martin **Dube**	Ministry of Education, Science and Culture of Mecklenburg-Western Pomerania, Schwerin, Germany

2. Guests

Representative of the relevant Federal government department

Antonius **Helou**	Federal Ministry of Health, Bonn, Germany

Representative of the relevant Länder *government department*

Michael H. **Wappelhorst**	Ministry for Innovation, Science and Research of the State of North Rhine-Westphalia, Düsseldorf, Germany

Representative of the Scientific Advisory Board

Peter **Nawroth**	Heidelberg University, Germany

Representative of the Leibniz Association

Heribert **Hofer**	Leibniz Institute for Zoo and Wildlife Research (IZW), Berlin, Germany

3. Representatives of collaborative partners (one-hour interview)

Michael **Piper**	Rector, Heinrich Heine University Düsseldorf, Germany
Joachim **Windolf**	Dean of the Medical Faculty, Düsseldorf University Hospital, Germany
Benedikt **Pannen**	Deputy Medical Director, Düsseldorf University Hospital, Germany
Martin **Hrabě de Angelis**	German Research Center for Environmental Health (Helmholtz Zentrum München) & German Center for Diabetes Research (DZD e. V.), Munich, Germany
Thomas **Illig**	Scientific Head and CEO, Hannover Unified Biobank, Hannover Medical School, Germany

15 May 2014

Annex C: Statement of the Institution on the Evaluation Report

German Diabetes Center (DDZ), Leibniz Institute for Diabetes Research at Heinrich Heine University Düsseldorf

DDZ would like to thank all involved persons for the excellent evaluation procedure as well as for the always open and constructive communication.

The Executive Board of DDZ read and discussed the Evaluation Report together with the directors of the institute and appreciates the detailed summary of scientific activities and the positive assessment of the departments of the institute. DDZ will be glad to follow the recommendations and advice given in the report.