

EURADIA Position on the Common Strategic Framework for EU research and innovation funding

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EURADIA, the Alliance for European Diabetes Research (www.EURADIA.org), seeks to ensure that developments in European research funding together with healthcare policy initiatives sufficiently address diabetes, one of the major grand challenges in health, which is having a major impact upon individuals, families, wider society and the economy of Europe.

A secondary goal is to use diabetes research as a case model for future strategy for biomedical research in Europe.

EURADIA is an Alliance of the leading diabetes research stakeholders working at the European level including academic scientists, people with diabetes, healthcare professionals and industry.

This position statement is based in part on the DIAMAP report. DIAMAP was funded under FP7 (HEALTH-200701) in response to a competitive call to develop a road map for future diabetes research in Europe. The DIAMAP project was coordinated by EURADIA and the complete report and accompanying brochure may be found at:-

www.DIAMAP.eu

This position is endorsed by the European Coalition for Diabetes (www.ECDIABETES.eu)

Executive summary

Preamble and goals: This document reviews the issues that span the breadth of diabetes research Europe-wide, with a particular focus on **general issues that can improve the efficiency of research and its translation to benefit the individual**. Also addressed are the **overarching roadblocks** identified through the discipline-specific concerns, along with **strategies and recommendations to overcome them**. There is no intention to recommend specific thematic areas for future calls for applications that are not considered relevant to the present public enquiry, aside from highlighting the need and justification for **including the general field of diabetes research as a top priority for European research**.

Priorities: this document focuses upon: policy, human resources, infrastructure, funding, societal and ethico-legal issues. **Recommendations** are provided with examples of key opportunities to improve the efficiency, competitiveness and impact of diabetes research Europe-wide, noting the communication and education strategies for implementation.

Policy at a pan-European level, within the context of health-related research must take action to address the diabetes epidemic, which is in part a consequence of escalating obesity driving type 2 diabetes but also reflects a disturbing increase in type 1 diabetes. Diabetes research should be more inclusively represented in European policies affecting all aspects of relevant health research and public health messaging. Diabetes is especially prevalent among the aged (>20% of individuals over the age of 65 [1]) and addressing this chronic disease must thus be a core component of future European policy for healthy ageing.

Human resources are vital, recognising the need to retain research talent in Europe and facilitate interchange at all levels of scientific and clinical endeavour through appropriate recognition and adjustment of equivalent career structures between countries.

Infrastructure will require the orientation of and accessibility to registries for patients, high-risk groups, biobanks and repositories, and clinical research networks that stretch Europe-wide. Ethical and legal issues need conformity to facilitate this approach towards international research collaboration. The proposed **European Platform for Clinical Research in Diabetes (EPCRD)** will provide essential services in this regard and will serve as a model for clinical research in other disease areas.

Funding sources mostly operate independently with few pan-European collaborations. Proposals to improve cohesion and integration of national funding structures require urgent consideration.

Dialogue between industry, academia, healthcare and non-governmental research organisations as well as government-funded bodies will be essential to optimise discovery, development and application of new medicines. International convergence of the regulatory framework for healthcare products would facilitate this process.

Societal and economic impact: the diabetes epidemic will have a catastrophic effect on healthcare provisions, which will pervade families, communities, cultures and economies, particularly impacting vulnerable groups. Initiatives to improve public health awareness are essential for effective implementation of recommendations from research.

Communication and education between scientists and healthcare professionals at an international level, and engagement of the general public and patients to empower personal decision-making are key implementation pathways for any integrative diabetes research policy.

Introduction

Europe urgently needs a comprehensive plan to rationalise, focus and integrate diabetes research to accelerate scientific discoveries and their translation into prevention and treatment. This is emphasised by the rapidly growing prevalence of diabetes in Europe, presently about 55 million and predicted to increase to over 66 million by 2030 [2].

The costs in human suffering (*chronic morbidity and premature mortality*) and the social and economic impact (*disruption to families, workforce and healthcare burden*) are huge and escalating [3]. Diabetes consumes about 10 percent of direct healthcare costs in Europe [4].

Diabetes in its two main multifactorial forms, type 1 and type 2 diabetes, afflicts people of all ages but the very young and the aged are of particular concern. **Tackling diabetes as a medical and societal catastrophe must thus feature prominently in the Research Grand Challenges of the European Union.**

Although many academic and healthcare institutions, charities, governmental bodies and commercial organisations are conducting or supporting diabetes research in Europe, **the impact is undoubtedly sub-optimal and often fragmented due to lack of a universally recognised cohesive plan** [5].

EURADIA, through The DIAMAP Road Map report [5], has assessed the current status of diabetes research in Europe, charted its future and identified crucial limiting factors (roadblocks) that impede specialism-specific advances and their translation into patient care.

Diabetes research Europe-wide was analysed by:

- reviewing current provision and future needs to support diabetes research
- identifying general roadblocks that impede progress across multiple specialism-specific areas
- assessing ways in which these roadblocks could be overcome.

Through the DIAMAP Road Map Report EURADIA recognises that there are often several viable options that may be taken to accomplish each objective. These can mostly be addressed using current national and European administrative frameworks, provided that appropriate adjustment, collaboration and integration can be undertaken. EURADIA therefore endeavours where possible *to identify the most practicable route consistent with the current and projected organisation of European science and healthcare*. EURADIA is also cognisant of the need for any strategy to be flexible and adaptable to respond promptly to new advances or changes in socioeconomic circumstances. Additionally, careful consideration has been given to the need for *a plan that enables on-going and future strategies to be addressed with continuity*.

Strengths and limitations of diabetes research in Europe

Basic and clinical science have each contributed towards most major advances in diabetes research. **Europe has strength in breadth and depth in all areas of diabetes research** relative to other global regions [6] and is also recognised for its innovation and quality of work in the fundamental scientific disciplines that provide the foundation for such research. However, **structure, funding and translation of this type of research are complicated by the composition and organisation of European Member States with their separate national procedures, highlighting the lack of interchangeability of 'process' across Europe**. This in turn limits integration, movement, cohesion and impact of effort between countries.

Individual experts from different countries are generally agreed on the importance of particular research programmes within specialisms, but opportunities to pool resources and derive critical mass within countries and especially between them are often prohibited by incongruities of funding, career structure and administrative processes. **The European Commission is acknowledged for making substantial progress to encourage and facilitate collaboration and integration of research at all levels across Europe**. Nevertheless, the amount of resource and strong national structures with limited flexibility continue to preclude full exploitation of the talents and willingness of organisations and individuals.

Diversity of career paths, funding and national research structures have been highlighted as major hurdles. The time taken to acquire funding and implement and manage research is disproportionately large compared with that devoted to the research itself.

1. Research policy

To the best of our knowledge research policy rarely transcends national boundaries except for the welcome (but inevitably limited and prescriptive) pan-European perspective of the European Commission Research Framework Programmes. Indeed, the majority of European countries have no formal research policy and only very few have a *bona fide* diabetes research programme. This contrasts with the USA where the National Institute of diabetes and digestive and kidney diseases (NIDDK) orchestrates the national diabetes research effort.

Enhanced concordance of research policy within the medical and healthcare sciences in general, and to include disease-specific disciplines, could be encompassed within a review of European national research activities. The level of discord noted in the EURADIA/DIAMAP Road Map report research and funding **survey emphasises the need to harmonise national policies without compromising local features (such as ethnic, cultural, family, or environmental factors).**

Other features of research policy that require coordination between countries are (among others) ethics, registries, and repositories/biobanks. Agreed procedures for accepted laboratory and clinical practice to facilitate policies should at least subscribe to the same requirements and general standards to ensure consistency and rigour.

The key elements of a *diabetes research policy designed for commonality across European countries* should include maximum integration of scientific and clinical training. This will ideally comprise specific components that accommodate the differing presentations of the disease and its complications in different genetic and environmental communities, and vulnerable groups.

The main policy priorities and recommended approaches towards harmonisation of European research policy include:

- integration of research and its applications, and interchangeability of structures and resources to optimise efficiency without stifling individuality of approach at the subject level.
- In addition to the European Commission Research Framework Programmes, dialogue between national medical research funding bodies in different European countries would be an example of a valuable facilitation step.
- Within the European Commission itself dialogue and enhanced collaboration between the different directorates impacting on health is welcomed. Academic-industry partnering at a multinational level would be a further means towards integration of all stakeholders in biomedical research, with consolidation of existing successful programmes such as the Innovative Medicine Initiative.
- There is an absolute need for a strategic approach to research supported by the European Commission with clearly identified priorities in keeping with needs of society on the one hand and available expertise on the other.
- European biomedical research priorities and the choice of specialised thematic focus areas must be based on strategic planning using a road mapping approach modelled on DIAMAP

2. Human resources

There is a strongly perceived need for greater congruity in the training, career structure, remuneration packages and status of individuals engaged in diabetes research across Europe.

Many bright young researchers from Europe elect to further their careers and use their experience gained within Europe in countries outside of Europe. For young investigators, this overseas stage in career development is often financed by the European country of origin, yet many of them never return to Europe. In addition to this 'skills drain' Europe is seen as a nursery that provides training for enthusiastic young scientists from developing countries. While Europe does not retain many of these individuals and does not gain the immediate benefit of the training given, this is not the intention. Rather, this activity is considered important for Europe's support of research in developing countries and should be continued.

Retaining our top talent and attracting back talent that has migrated are key requirements for continuity of high-level basic and clinical science. China has been very successful in this regard; Europe has not. This is probably best achieved through a more consistently structured career pathway for scientists at early doctoral level. Such a pathway should accommodate the need for clinical scientists to undertake laboratory-based research interspersed within a clinical curriculum and career structure. Examples of potential advances would be:

- a) clinical training rotations to include periods of laboratory-based or other non-ward based research
- b) extended contracts (currently often only 3 years) to more than 5 years to enable both training and its application in an integrated manner.

Incorporated within the need for greater consistency of career structure is **greater conformity of professional recognition and remuneration at equivalent rates.** The disparity and disconnect between basic and clinical science discourages interchange between these two arms of research and between equivalent grades in different countries.

3. Funding structures

Several established funding structures support biomedical research in Europe, taking diabetes as the model (Table 1). Each offers welcome features but experiences limitations that impinge upon pan-European collaboration and concerted effort. European Commission Framework Programmes (FPs) and national government funding provide a base level of financial commitment, but this is perceived as insufficient for *more ambitious programmes to adequately address unmet needs*. Funding sources also vary with regard to the type of research they support. We note and appreciate the welcome and large increase in FP7 funding.

Table 1. Current funding sources and perceived limitations for diabetes research

Source of funding	Perceived shortcomings
European Commission Research Framework Programmes (across the European Union)	calls can be too variable (some are too broad, others over prescriptive) calls with non-scientific criteria can lead to large consortia, with challenges for coordination, administration and focus: the example of unwelcome and obligatory involvement of SMEs regulations on reporting, heavy administration no continuation of projects
National government funding	national interests; research policies coordination between countries lacking
Non-profit foundations and organisations	funding rarely pan-European limited resources, often for pre-specified use
For-profit organisations	issues of: transparency, independence, regulation/legislation, intellectual property, profit
Industry	often limited to pre-specified areas; IP issues

Specific issues pertaining to European Commission and national government funding

Concerning the European Commission and national government funding, these should support both basic and applied clinical research, including research on effectiveness of implementations in healthcare and translational medicine. Compared to the current situation, there should be a greater variability in European Union-level funding instruments tailored to the specific needs of the European research community as well as corresponding to the requirements of regional (EU) and national research strategy. Most notably, these should contain more career-promoting funding opportunities, including support for mobility of researchers within Europe and also worldwide. Academic careers and research need to become more attractive to healthcare and medical professionals.

In order for European Commission support for biomedical research to be truly effective, it must be highly focused with priorities based on research strategy (the road map approach described above). It must not be diluted and compromised by the effort to solve unrelated societal issues. The Commission should be seeking through its biomedical research programmes to address the grand challenges relating to the health and wellbeing of citizens of Europe, and to enhance European excellence in research. These programmes should not be compromised by a misplaced focus on the for-profit sector and most specifically SMEs. **Full involvement and direct support for private enterprises, regardless of their size, should be encouraged on a case-by-case basis where the enterprises can offer unequivocal added value in terms of research expertise. It should never be obligatory.**

National government funding sources often focus on current national interests and research policies, leading to heterogeneity in research funding at EU level. Potentially, increasing coordination of these instruments on research issues common across the EU could increase synergy and collaboration.

Research organisations are increasingly moving towards full-cost (total cost of all *resources* used or consumed, including direct and indirect costs) implementation of funding, and European Union and national governmental funding sources should support this. This will also increase the long-term financial stability of research groups and allow for more sustainable research planning. Ways to increase collaboration between academia and the pharmaceutical industry deserve greater exploration, taking into account issues of transparency and independence.

To be effective, European funding for diabetes research must evolve towards an integrated approach that is based on a clear scientific vision and that allows for coordination between all funding bodies. Adherence to a road map strategy (the EURADIA/DIAMAP model) with improved communication between European funding agencies and industry offers a unique opportunity to achieve this.

Direct partnerships between the European Commission and non-profit funding organisations are strongly encouraged. This allows for reciprocal “leverage” of funds, always provided that there is communality of research priorities. Several concerted initiatives have demonstrated the value of industry-sponsored (unrestricted, educational) grant-type projects proposed and led by principal investigators in academic and clinical institutions. The European Foundation for the Study of Diabetes (EFSD: www.europeandiabetesfoundation.org) provides an established example of this type of operation with a true partnership between a private non-profit funding agency and pharmaceutical companies. The model is well justified by the enthusiasm with which it has been embraced by industry and the academic research community; with rigorous peer-review process paying close attention to the research-based issues of design, methods, analyses and novelty.

While the major emphasis of this type of collaboration seeks to improve understanding of fundamental pathophysiology, conceptual approaches to disease management are accepted as a part of the programme, and the identification of novel therapeutic targets might reasonably be anticipated from some studies. Given the success of this format by EFSD, the challenge is to marry such programmes into a more co-ordinated framework Europe-wide and to complement the more thematically driven ‘calls’ from the European Commission and national bodies. The award of grants is a competitive process, which ensures rigour of project and personnel but there is often not sufficient resource to fund long term. **Partnerships involving industry, non-profit agencies and the European Commission would provide a “third way” for improved funding of biomedical research in Europe.**

Complexity of the application procedure leads to discrimination: The European Commission Framework Programme grants are now creating a separate industry of companies that will advise universities find commercial partners, and help write and present applications and manage them. While this may assist some of the larger bids, because these companies are expensive they may be driving out the smaller and more academic pure research that was intended to be an important foundation component of the Frameworks. In consequence many applications have commercially orchestrated undertones that detract from the more fundamental science and medicine that is necessary for major advances. There is the real risk that ‘grantsmanship’ may be rewarded rather than scientific vision and expertise.

Sustained support for excellence is a prerequisite for a competitive European Research Area. **Any future European Commission research programme will need to include the possibility of continued funding for the most successful projects in order to guarantee optimal return for investment.** A small percentage of the total programme budget should be reserved for this purpose. Only the most successful projects/teams would be offered the opportunity to apply for continued funding, always subject to rigorous peer review. Such an opportunity should not depend upon a future call in the same area of research as is the case at present.

4. Coordination and implementation of European research policy

Infrastructure for research incorporates all aspects of the clinical and basic scientific educational process, career paths, institutional operation, and resource implications necessary to support advanced research at a multi-national level.

The lack of compatible infrastructures Europe-wide has been identified as a major roadblock in several important areas of diabetes research. Concentrating resources and combining efforts in several scientific areas, particularly infrastructure, would create a solid basis for cutting-edge research in diabetes. In building this structure care should be taken to include sufficient flexibility for efficient and creative work in smaller research units. Overall the infrastructure needs to provide a balance between uniformity and individuality. The development of a sustainable and efficient infrastructure will require a thoughtful process of harmonisation in various areas, such as ethics, legal and financial issues, as well as previously considered issues of human resources and funding.

Due to the diverse nature of the disease and its far-reaching implications, research in the field of diabetes must be conducted in numerous different settings and locations within academic institutions, hospitals, primary care, public health and industry to ensure connection between discovery, development and implementation.

In this context it has been helpful to take advantage of recent and well-considered proposals for infrastructural changes to facilitate research in biological, biomedical, behavioural and socioeconomic sciences in Europe such as:

- the European Strategy Forum on Research Infrastructures (ESFRI) (<http://cordis.europa.eu/esfri/>)
- the proposed Road Map Initiative for Clinical Research in Europe (EFGCP) (<http://www.efgcp.be>)
- draft documents such as the European Medicines Agency (EMA) Road Map (<http://www.ema.europa.eu/htms/general/direct/roadmap/roadmapintro.htm>).

Overall organisation of diabetes research in Europe: the European Diabetes Academy

The European Commission is recommended to consult with learned bodies to develop a European 'overarching diabetes research infrastructure' as these organisations have contact with all diabetes stakeholders with an interest in research, while acknowledging the primacy of individual national identity. A central entity should be created, the **European Diabetes Academy** that would ensure coordination and establish Europe-wide diabetes research policy. The Academy would be responsible for oversight of the regional research effort and ensure the required coordination. It would be responsible for following up adoption of the DIAMAP road map strategy and monitoring the impact on individuals with diabetes.

Existing policy, procedures and regulations concerning identification of thematic areas of research for support by European Commission Framework Programmes are considered somewhat burdensome and occult by the research community. Despite the obvious commitment of the Commission to biomedical research across Europe, including diabetes, there are unusual constraints imposed by the principle of subsidiarity. To ensure the most rational use of precious European funds and to allow for development of a comprehensive plan for diabetes research there is an urgent need to involve specialists as impartial advisors to the Commission, providing balanced guidance for selection of topics for grants and a pool of expert reviewers acting above national concerns. A roster of leading diabetes research experts (as part of the **European Diabetes Academy**) based on the model currently under development for cancer would be suitable for this purpose. Members could be elected by elite national scientific academies (e.g. Royal Society in the UK; Académie des Sciences in France) based on scientific excellence, ensuring an equitable spectrum of expertise to represent the full diversity of diabetes research exemplified in the EURADIA/DIAMAP Road Map Report. The Members of the Academy would comprise a fully independent, elite body recognised for its academic qualities and competence.

5. The special case of clinical research: European Platform for Clinical Research in Diabetes

Within the European Union there are increasing numbers of adults and children with diabetes. Despite guidelines and consensus statements related to approaches, targets and therapies, across Europe there remains huge variation in the quantity and quality of diabetes-related clinical research and health care available for people with diabetes. This variability in research activity and service delivery is a consequence of many factors, the most significant being the social and cultural differences among countries, differences in clinical governance, and lack of structured networks of interested parties with commonly agreed goals.

DIAMAP emphasised the urgent need for a central resource to facilitate European clinical research in diabetes. This resource, referred to hereafter as the European Platform for Clinical Research in Diabetes (EPCRD) is envisaged as a joint initiative with support from the Commission, the private sector and non-profit funding agencies. This platform for clinical research in diabetes can serve as a model for other disease areas deemed by the Commission to be facing similar challenges.

Justification for the EPCRD and advantages for society

There are many existing networks and study groups that are investigator-led, focussed upon specific research areas and funded by individual membership, research grants or the pharmaceutical industry. Such networks have developed a way of exchanging, learning and sharing of research ideas and best practices across Europe. Often these networks disperse when the grant comes to an end. This proposal is to access these networks and experience and to develop a more extensive and all-encompassing network with a central point of organisation.

The concept of a European Platform for Clinical Research in Diabetes (EPCRD) is based on the understanding that people living with diabetes and their families will find it relatively easy to understand its value to improve diabetes care. The support of the European population is essential and offers a significant opportunity for transparency in determining how diabetes research budgets are spent. The key to the success of the EPCRD is the role and consent of the individual person with diabetes. Modern technology has revolutionised the access to all sources of information for individuals, across all traditional borders of language and to some extent culture and education. Individual patients and their representative organisations will provide the impetus and drive to develop the EPCRD, once the network is initiated.

A large population of people with diabetes with variations in genetic and ethnic background (and family members) could be made accessible to clinical (and basic) researchers and the sponsors of research by participation in a network with a centralised point of entry. The DIAMAP road maps have repeatedly mentioned as roadblocks the need for registries of people with diabetes, networks of specialist researchers, access to biobanks and human biological material (especially in relation to the rarer complications) and the need for more standardised evidence-based treatment guidelines. The majority of roadblocks are addressed within the Horizontal Issues report by engaging with organisations or individuals external to the research community. However, it was felt strongly that diabetes research would be enhanced if the clinical research community itself could drive a collaborative initiative as it deals with the consequences of research upon treatment and care delivery (this Goal is linked with many Goals and Milestones throughout the road maps).

European clinical research has limitations compared with the United States in that access to large numbers of people with diabetes and healthy volunteers with specific characteristics in single centres is difficult. Clinical research, from small studies to large-scale pharmaceutical trials, or research into health service provision is more laborious and less representative than it could be because of the number of countries, languages and organisational cultures. The EPCRD would facilitate research in such situations.

Major aims of the EPCRD:

- Facilitate and enhance clinical diabetes research with the purpose of improving care and treatment for people with diabetes.
- Facilitate access to data and biological samples by providing a uniform agreed and ethically approved infrastructure to permit sample and data sharing across multiple national and international security barriers.
- Improve access to structured education and training for European diabetes researchers and healthcare professionals engaging in research activity, and for people living with diabetes.
- Create centrally determined governance structures in line with current ethical guidelines.
- Facilitate access to information and online databases of clinical studies and trials, thus encouraging participation by interested volunteers (with diabetes and without). The closer dialogue between professionals and research participants is intended to encourage greater understanding of the science.
- Streamline the processes for dissemination of research findings through a dedicated communication channel including a consultation process with people with diabetes and the public.
- Encourage investment by and participation of industry, facilitating access to a large number of research subjects and to scientists from sub-specialties. Funding of industry-initiated trials could be standardised across Europe supporting the concept of the 'European diabetes patient'. The use of such a market approach to clinical research has the potential to drive down costs to increase the competitiveness of Europe as a clinical trial location.

Legal and statutory requirements associated with repositories and databases will need to be considered in the context of privacy protection. The boundaries between ethical and legal issues may be blurred but it is anticipated that advances on a Europe-wide level will not be shared equitably until there is greater congruity in the documentation and procedural requirements for research approval and practice.

Holistic care for people with diabetes requires interdisciplinary and experienced management usually delivered according to guidelines, local resources and where possible patient expectations. In 'person-centred care' individuals can determine their own self-management priorities based on comprehensive training and education. These personal priorities can differ from the evidence-based targets that are frequently used to determine the quality of care delivered. From an ethical point of view, further discussion may be necessary to delineate some apparent tensions between personal choices and evidence-based targets.

The management of people living with diabetes implicates substantial maintenance of (electronic) medical records (perhaps more so than many other chronic diseases). These contain personal and sensitive information, aiming to help healthcare providers to deliver appropriate levels of care and that is important for the purposes of research. However, medical files also might be used for extraction of performance indicators, assessing the quality of the delivered care, and sometimes leading to additional payments for performance. This disconnection between 'real' care and 'idealistic' care needs ethical rationalisation and this also applies to use of information for research. Permission and acceptance of patients for use of their (anonymous) medical information for objectives other than performing good medical care needs reflection and clarification. This will be implicit in the development of detailed data repositories and will have to be addressed transparently and ethically by the EPCRD.

6. Communication and education

Transparency, public awareness and health literacy have been discussed as important areas for communication to enhance interest and support in biomedical research. Communication between scientists and healthcare professionals is not particularly a roadblock but it is an area that requires growth in line with technological advance if full advantage is to be taken of the opportunities to disseminate knowledge. Examples of inter-professional communication include open-access journal publishing and information retrieval, which would circumvent some of the current limitations.

Using the model of diabetes, education in its various forms represents a fundamental objective of communication that will deliver advancements to the patient. For example, humanities of care, which takes critical account of the human condition in ill health, may assist patient empowerment and the transformation of information to patient decision-making.

It is the responsibility of everyone involved in research to contribute to public understanding and appreciation of the value of knowledge advancement and its application. The many established and new media outlets offer a powerful expanse of opportunity for advocacy to engender a public environment conducive to the support and advancement of research. Participation in media events and production of publications to inform the public of research activities are already requirements of many funding bodies. This in turn will form an integral part of a two-way exchange that will foster public engagement in research including participation in clinical trials.

New media and its importance to research

The Internet provides a powerful opportunity for discourse between researchers, continuing medical education, and the dissemination of research information to enhance public awareness. Telehealth in particular offers a new conduit for real-time interactive distance collaboration in research and this might include remote patient consultations and monitoring (with appropriate ethics and confidentiality requirements), shared methodological and analytical research and extended access to more isolated communities and research centres. Further research into distance education (e-learning) and its applications for patient awareness and self-care is warranted.

Public involvement in research

Although research across all fields is now more accessible to the general public there is always a need for more direct involvement through consultation and participation in clinical trials. This could foster greater dialogue and enhance 'transparency'. Increased patient involvement and increased education of the public on research advances could be facilitated by organisations such as EURADIA, EASD and IDF-Europe.

7. Regulatory issues and dialogue with industry

Regulatory framework for new medicines

Probably the most significant and life-saving steps in the management of diabetes have arisen from the translation of basic research into therapeutic modalities. Yet, new and effective medicines for the prevention and treatment of diabetes and its complications are urgently needed. This is illustrated by the continuing rising epidemic of diabetes, the failure of conventional public health messaging, and the difficulty experienced in trying to contain the disease process even with the selection of agents and devices presently available.

This need for new and different therapies is well appreciated by the regulatory agencies at international level [e.g. European Medicines Agency (EMA)] and national level. However, safety is paramount, and the need to ensure that the risk:benefit analysis is justifiably favourable is often interpreted as a protracted and unnecessarily tedious process. Indeed, regulatory registration trials often require substantial multi-national collaboration. These studies are inevitably expensive: success is far from certain, and on-going commitments are difficult to predict. The statistics quoted for these aspects of pharmaceutical activity are quite variable, but conservatively only one in several hundred promising preclinical compounds is ever likely to be developed into clinical assessment beyond phase 1. Thereafter, less than one in 10 compounds studied thoroughly at phase 1-2 clinical level will be carried forward into phase 3. Thus a major cost to large pharmaceutical companies is clinical trials of agents that are not continued. For a drug to reach approval an investment of around 1 billion US dollars is often considered as a reasonable (if unconfirmed) estimate. In consequence the lower risk strategy of 'me-too' drugs is favoured in which further minor variants are developed within a class where outcomes have already been demonstrated. The pharmaceutical industry has sometimes voiced this concern and suggested that greater incentive is required to speculate in the development of entirely new types of agents. A greater guarantee may therefore be required for the pharmaceutical industry. For example, a successful new medicine might be allowed sufficient patent life (or exclusivity licence) to enable reasonable investment to be recovered and reasonable reinvestment to be available for development of future medicines.

While it is not in the remit of this document to explore the financial basis of pharmaceutical investment it would seem logical to encourage *international conformity of trial design and greater harmonisation of requirements for marketing authorisation* to ensure that the same trials are suitable to each of the major regulators [e.g. European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA)].

Pharmaceutical industry

It must be acknowledged that the recent development of new anti-diabetic therapies has been dominated by the larger pharmaceutical companies and this is likely to continue for the foreseeable future. However, even cursory examination of the origin and early development of more recent therapies reveals that the basis for the identification of 'drug targets' and the templates for new therapeutic modalities have been heavily reliant on the advances of basic and initial translational research from largely academic scientific sources. Within the framework of ESFRI (European Strategy Forum on Research Infrastructures) several important projects (EATRIS, European Advanced Translational Research Infrastructure; ECRIN, European Clinical Research Infrastructures Network; EU-OPENSOURCE, European Infrastructure of Open Screening Platforms for Chemical Biology) have been initiated that aim to improve European research in the field of preclinical and clinical drug development.

Small pharmaceutical and biotech companies and enterprises funded by venture capital are often at the interface between academic sources of the fundamental science and licensing of 'proof of principle' studies and new chemical entities. Moreover, collaborative studies in which pharmaceutical companies have engaged with academic, scientific and clinical institutions have provided the wealth of necessary mechanistic (mode of action) studies to enhance the understanding of new agents and to identify ways in which they can be most usefully employed. The large phase 3 clinical trials to demonstrate efficacy and provide the basis for the 'indications' are inevitably at the behest of the regulators and the expense of the industry. Beyond this, the larger 'safety' studies that often now require extensive post-authorisation commitments are mostly driven by regulatory requirements and at the expense of the industry. It is noted that the pharmaceutical industry in general is showing particular vigilance given the damaging effects of unforeseen (and often unforeseeable) adverse effects.

As mentioned above, European Commission support for industry-based research, large and small, is to be encouraged on a case-by-case basis when deemed appropriate and likely to accelerate discovery in a specific milestone-driven research track: it should never be a goal in and of itself.

Food industry

The food industry (and by extension the agricultural sector) has a huge impact on the development of obesity and the availability of healthy foods to the population. The market share for functional food has expanded during recent years but scientific validity of many health claims remains unconfirmed. Claims should be evidence-based, validated with studies conducted according to Good Clinical Practice to avoid misleading consumers. In addition, there is a need for the display of scientifically correct information on food labels across Europe in a consistent and understandable format. An area of research in itself is the possible link between food label information and dietary intake.

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