

Medical & Scientific Advisory Panel (MSAP)

Terms of Reference

1. INTRODUCTION

Summary

The DEBRA International Medical and Scientific Advisory Panel (MSAP) provides expert independent scientific advice to DEBRA International ('DI') via the DI Head of Research.

In 2019, the key research-active national DEBRAs founded the EB-ResearchNetwork (EB-ResNet) which focuses on support of EB research and its clinical development. DEBRA International is one of its member organisations and there are also non-DEBRA EB patient organisation members of the network. Since the foundation of this platform, research-support and management activities are coordinated by EB-ResNet.

EB-ResNet works on behalf of its members to coordinate and promote best-practice research support among its members.

MSAP's main role is to help guide DI's approach to effective support for research to benefit all people with EB. This includes advice on:

- EB research priorities to improve understanding of EB and thus create concepts for effective treatments, and their development.
- the best-practice processes for evaluation of both research proposals and progress of funded research.
- whether or not individual research proposals merit support by DI or national DEBRA members that are funding research, in pursuit of DI's mission, according to established DI research priorities, and agreed criteria.
- the importance and relevance of developments in other fields and novel approaches to furthering EB research.
- the direction and scope of DI research strategy to attract relevant, high-quality research proposals, in achieving DI's goals.
- other advice on EB research matters at the request of the DI Head of Research.

MSAP was set up by the forerunner of DI, and its members are senior EB researchers and clinicians recognized for their expertise and experience of EB; additional researchers with relevant dermatological research knowledge broaden the knowledge base.

MSAP members are rotated to ensure that the MSAP reflects emerging directions of research and advances in knowledge and technology, with appointments made by DI Head of Research in consultation with MSAP.

Membership is voluntary and not remunerated, with only economy travel expenses associated with attendance at MSAP meetings reimbursed.

Purpose of this MSAP Terms of Reference (ToR) document:

This document defines the authority, purpose, membership, function and general operation of the DEBRA International (DI) Medical & Scientific Advisory Panel (MSAP). DI works on behalf of its membership of national DEBRAs within agreed frameworks to maintain high standards in research and best practice in research support.

(NB: for avoidance of doubt, 'DEBRA' and 'DI' should be taken to mean DEBRA International, or its forerunner; individual national member DEBRAs will be referred to as such. DI is a member of EB-ResNet as are several research-active national DEBRAs and other EB patient organisations.)

2. AUTHORITY

- 2.1.** MSAP is a voluntary independent expert advisory panel established by DI.
- 2.2.** MSAP has an advisory role only to DI, which takes MSAP advice for its own purposes, and on behalf of its national DEBRA members which support research.
- 2.3.** MSAP has no executive role either in DI or in any member DEBRA.
- 2.4.** MSAP is managed by the DEBRA International Head of Research.
- 2.5.** DI and national member organisations remain the ultimate decision-making body on the strategic direction of research.
- 2.6.** The ultimate decision-making body on the funding of research is DI, or the Boards of national member DEBRAs, whichever is providing the research funding: both DI and national member DEBRAs will give due regard to funding recommendations received from MSAP. Where a national member DEBRA has an overriding reason (e.g. building national EB-research capacity, or defined unmet clinical need) for funding research considered by MSAP to be of 'national standard', but not 'international standard' (see [Appendix 2](#)), any serious fault with research methodology raised by MSAP or DI is communicated back to researchers, and should be remedied before the research is funded.
- 2.7.** National member DEBRAs may request the assistance of MSAP in national grant-making schemes via DI Head of Research; MSAP may accept or decline to review additional national grant schemes. Individual MSAP members may accept to assist as independent scientific/ clinical experts, i.e. not representing MSAP.
- 2.8.** While MSAP makes recommendations in good faith to DI, based on objective evaluation of information made available to them by DI, and drawing on their own knowledge and expertise, MSAP is not liable in any way for the decisions, including funding of research, made by DI or national member DEBRAs, whether acting on the recommendations of MSAP or not.
- 2.9.** MSAP members receive no remuneration for their activities, but are reimbursed for expenses incurred (e.g. accommodation, economy travel) as part of their MSAP duties performed at the request of DI.

3. ROLE AND FUNCTION OF MSAP

- 3.1.** MSAP was created by DI to provide a source of expert advice both on the clinical and scientific research priorities in DI's quest to find effective treatments for people with EB, and on the scientific merit and likely patient benefit of funding particular research proposals received by DI.

- 3.2.** MSAP provides advice as requested, to help guide identification of strategic priorities and appropriate initiatives in support of symptom-relief research, as well as in research targeting the causes of EB to develop curative treatments.
- 3.2.1** MSAP provides comment and input to the DI research strategy, revised by DI approximately triennially, to help ensure that the strategy reflects advances in EB knowledge, and wider biological understanding and technology development, and targets opportunities and barriers as appropriate for DI.
- 3.2.2** MSAP recognizes DI's role as a patient organization responding to its membership, and hence DI's need to balance provision of support for people with all types of EB, in current and future generations.
- 3.3.** MSAP's main routine role is to act as an advisory body for DI's centralised peer-review of research-grant applications received by DI, as managed by DEBRA International Head of Research, and to advise on the progress of research grants.
- 3.3.1** The basis of all grant evaluation in any reputable medical research charity is peer review - that is, the process of obtaining independent, expert, opinion on research proposals and reports received by the charity, and the making of recommendations to the charity.
- 3.3.2** Peer-reviewers are selected by the Chair/ Deputy Chair of MSAP jointly with the DI Head of Research; individual MSAP members may be asked for advice in identifying possible reviewers in their own areas of expertise.
- 3.3.3** Grant applications normally are reviewed by two MSAP members and at least two external experts.
- 3.3.4** MSAP members will score applications according to the scheme noted in [Appendix 2](#).
- 3.3.5** MSAP receive interim and final progress reports on research projects, and may be asked for specific advice about remedying issues with ongoing grants. Individual MSAP members, selected by DI Head of Research for their knowledge, are asked to provide formal written review of final reports.
- 3.4.** MSAP makes recommendations in good faith according to DI's stated research priorities, and the key criteria agreed with DI:
- scientific quality and innovation;
 - feasibility of the proposed research and its value for money; and,
 - relevance of the proposed research to the medical condition EB.
- 3.5.** MSAP therefore:
- acts as guardian of scientific quality and relevance to people with EB of the research funded by of DI and the national research-funding DEBRAs.
 - is central to maintaining the reputation of DI and the national research-funding DEBRAs among the academic and clinical research community, and bioindustry, and research sponsors and donors.
- 3.6.** Should DI issue a call for research proposals with a particular focus within its overall stated research priorities, or make any change to its research priorities, MSAP will be informed in sufficient time to take the changes into account in its evaluation of proposals, or to raise with DI any concerns it may have in its ability to carry out the evaluation according to the standard agreed criteria.
- 3.7.** MSAP makes recommendations on the selection for funding of suitable research grant applications via the DEBRA International Head of Research to DEBRA International and thence to Trustees of member DEBRA organizations, which make

the decision on funding of research based on funding availability, unmet clinical need and national priorities.

- 3.8. MSAP considers all research-grant applications, regardless of the country of submission, and possible funding availability, under the same criteria of research quality, value and relevance to EB.

4. MEMBERSHIP

- 4.1. MSAP membership is drawn from the senior academic and clinical research community, primarily but not solely from the EB research and clinical community.
- 4.2. The membership of MSAP reflects the breadth of research and clinical expertise and opinion required to address DEBRA's research priorities.
- 4.3. MSAP membership is selected on the basis of individual members' expertise and track record in relevant areas of research.
- 4.4. MSAP's expertise is the sum of individual MSAP members' expertise: members are chosen to ensure that there is at least one member able to provide an expert view on each core area of DEBRA's research priorities.
- 4.5. Membership of MSAP is reviewed annually (usually at the summer MSAP meeting) to ensure that its expertise reflects current and emerging technologies and directions of research, and geographic representation of countries engaged in EB research.
- 4.6. A Patient Representative will be appointed by DI as a MSAP member (see [Appendix 3](#) for role of patient representative)
- 4.7. The number of members at any time should be between 9 and 15 (excluding the Patient Representative member, any ex officio members, DI staff, or invited observers, none of whom has rights on the scoring of research proposals).
- 4.8. The Head of Research of DEBRA International is responsible for making appointments and asking members to step down. Where appropriate, this will be in consultation with the MSAP Chair and Deputy Chair and, where timely and feasible, with current MSAP membership, and national DEBRAs on whom there may be an impact.
- 4.9. The Chair and Deputy Chair are to be appointed by mutual agreement between DI Head of Research in consultation with national research-funding DEBRAs, and MSAP members.

5. TERMS OF OFFICE

Members

- 5.1. The term of membership of MSAP is normally 4 years (or 8 research calls, whichever is greater).
- 5.2. A member of MSAP may serve for not more than 3 terms of membership (i.e. 12 years)
- 5.3. However, a member of MSAP should not serve more than 8 years consecutively; after stepping down, a former member may be reappointed after 2 years.
- 5.4. If, in the joint opinion of both DI Head of Research and the Chair of MSAP (in consultation with the full MSAP membership), an individual member has expertise

essential to MSAP that cannot be met by new candidate members, that individual may be invited to serve additional time.

Chair and Deputy Chair

- 5.5.** The Chair will normally be appointed by DI Head of Research from among MSAP members who have served at least 2 years (or participated actively in at least 4 grant rounds, whichever is greater). The Chair's term will last 3 years (or 6 rounds, whichever is greater).
- 5.6.** The term of Deputy Chair is also 3 years (or 6 rounds, whichever is greater). The Chair, and the Deputy Chair, may serve an additional term, as an ordinary member of MSAP, thus extending their consecutive membership time.
- 5.7.** If, in the joint opinion of both DI Head of Research and the Chair of MSAP (in consultation with the full MSAP membership), the Chair or Deputy Chair's role cannot be met by candidate members, the existing Chair may be invited to serve additional time.
- 5.8.** Where the Chair resigns, retires or otherwise ceases to be Chair during the year, the Deputy Chair assumes the role of interim Chair until the new Chair can be appointed. The Deputy Chair does not automatically become Chair.

6. MEETINGS

- 6.1.** MSAP members usually meet twice each year (depending on the number of research-grant rounds funded), in a venue to be agreed, usually London or Vienna.
- 6.2.** Meetings are usually held the first or second Monday of June and December each year, with the date confirmed usually ~6 months ahead, or as decided at the previous MSAP meeting. In the case of additional, or altered timings of meetings, MSAP members will be informed by DI of the date and venue as far in advance of meetings as possible
- 6.3.** The main purpose of meetings is to:
 - 6.3.1** Consider grant applications and external peer-review opinions sought by DEBRA International Head of Research.
 - 6.3.2** Provide advice or address research prioritization, DI research strategy, peer-review, or other relevant issues raised by DI Head of Research or the Chair of MSAP.
 - 6.3.3** Consider, as appropriate, annual research-grant progress reports, and final reports, to assess progress and any remedial action or advice required. Reports cover the work undertaken, the results achieved, comparison of actual results to those anticipated in the application, an explanation for any discrepancies and any other relevant information. The information required in both the interim annual and final reports is detailed in a document made available to all grantholders, and on the EB-ResNet website. These reports are received by the DEBRA International Head of Research, and then discussed as appropriate with the MSAP Chair, Deputy Chair, and other MSAP members.

7. QUORUM

- 7.1.** At least two-thirds of the active MSAP membership must be present at any meeting, and the members present should have the combined expertise required to allow expert discussion and decision-making.

- 7.2. Should either less than two-thirds active membership be present at a meeting, or insufficient joint expertise be available among the members present, then the Chair (or Deputy Chair, if the Chair is not present) will make the decision on whether to proceed.

8. CONFLICT OF INTEREST

- 8.1. Owing to the relatively small size of the global EB research and clinical communities, and high level of collaboration among their members, MSAP and DI must be particularly vigilant in considering issues presenting any possible conflict of interest.
- 8.2. The DI Head of Research will (in consultation with the Chair, or Deputy Chair, of MSAP where appropriate) consider whether any research proposals, research reports, or other information, may give rise to a conflict of interest, prior to documents or information being sent to MSAP members. Any MSAP member receiving information which he/she feels presents a conflict of interest will immediately alert DI Head of Research and, as appropriate, the Chair of MSAP.
- 8.3. Each meeting will start with the Chair asking MSAP members, and other attendees, whether they have a conflict of interest in any item on the agenda. Any MSAP member, DI staff or observer, with a conflict of interest in any matter under discussion must declare a conflict of interest and excuse themselves from consideration of any such items; in most cases, this will require the individual to leave the room, but this is at the discretion of the Chair of MSAP and DI Head of Research.
- 8.4. As many MSAP members are themselves active researchers, and may submit grant applications to DI, they will excuse themselves from consideration of any proposal submitted by themselves, or a member of their laboratory or department, or close collaborator from another institution, or any such individuals where there has been a close relationship historically, especially within the past 5 years.
- 8.5. MSAP members with industry links, remunerated or not, which might affect their impartiality in judging any particular application, must declare those interests and excuse themselves from consideration of proposals or research reports.
- 8.6. MSAP members with close personal, family, or professional connections, which might affect their impartiality in judging any particular application, must declare those interests and excuse themselves from consideration of proposals or research reports.
- 8.7. Grant applicants and grant holders are able to request that specific individual researchers (including MSAP members) or research groups do not review grant proposals, or receive reports, for reasons of research competition, and DI and MSAP will respect these requests.
- 8.8. MSAP members will excuse themselves from consideration of any proposal or report for any other reason where they feel they have, or may have, a conflict of interest, and inform DI Head of Research and if appropriate, the Chair of MSAP, of the reason.
- 8.9. If any MSAP member has any doubt about whether an issue presents a conflict of interest, either for themselves or for any other member of MSAP, then they may raise it in confidence with DI Head of Research, and or the Chair or MSAP, or raise it for discussion by all MSAP members at an MSAP meeting. Any difference in opinion regarding conflict of interest will be reviewed and the outcome determined by the DEBRA International Head of Research.

9. CONFIDENTIALITY

- 9.1.** MSAP members agree to follow the principles of confidentiality during MSAP meetings and in any correspondence relating to meeting business.
- 9.2.** MSAP members agree to not disclose any confidential and/ or personal information received from DEBRA with any third parties and to meet requirements of the General Data Protection Regulation (GDPR) and Austria's Data Protection Law 2018. DEBRA International is registered in Austria as non-profit organisation. Confidential information would include information included in research grant applications and progress reports, opinions expressed or recommendations made to DI on what research to fund, and information provided by peer reviewers. Personal data must only to be used for the purposes of assessing the research-grant application.
- 9.3.** The same requirements for confidentiality and compliance with regulations apply to MSAP members' personal data. Individual members of MSAP, agree that DEBRA may contact them in relation to their role as members of MSAP, or for the purpose of requesting ad-hoc advice on specific issues relating to EB research as appropriate to their expertise, or to inform them about DEBRA research initiatives or events.
- 9.4.** DI staff and any observers invited to attend MSAP meetings with the approval of the MSAP Chair and DEBRA International Head of Research, or in receipt of confidential research documents or related information, agree to observe the same principles of confidentiality
- 9.5.** Maintaining confidentiality in the peer review process is essential: reviewers provide candid comment on the assurance that their identity will only be disclosed to those directly involved in the decision-making process and not to the applicants.
- 9.6.** Applicants will be sent the anonymised comments of peer reviewers and recommendations of MSAP to help successful applicants make minor adjustments to their workplans as necessary, and to help unsuccessful applicants understand why they have not been recommended for funding and to improve future applications and research.
 - 9.5.1** the only information provided by reviewers that is passed to applicants is that on the peer-review report forms marked as information to be passed to applicants.
 - 9.5.2** peer-reviewers are advised that they may provide any additional confidential information, for consideration by either DI staff and/or MSAP, separately to the DI Head of Research, and this will not be disclosed to applicants.

10. MINUTING OF MEETINGS

- 10.1.** Proceedings of meetings, and recommendations made, will be minuted by the DI Head of Research, and approved by the Chair MSAP.
- 10.2.** Any details of discussion or recommendations which would need to be kept confidential from individual MSAP members will be omitted from the minutes, and only the overall recommendation/ conclusion recorded.
- 10.3.** Details of any confidential concerns relating to individual grants/ research will be recorded in the grant record.
- 10.4.** Minutes (or summaries of minutes) will be made available to DI, and national research-funding DEBRAs.

11. ACCESS TO MEETINGS

- 11.1.** The DI Head of Research attends all meetings, for the purpose of representing DI, recording proceedings and recommendations, and clarifying any issues raised by MSAP on research grants or management. The Head of Research does not score research proposals, and does not contribute to quorum.
- 11.2.** The Patient Representative is a member of MSAP, attends all meetings to represent the views of people with EB. The Patient Representative does not score research proposals and does not contribute to quorum.
- 11.3.** DI staff and Trustees of national DEBRAs may be invited to participate at the discretion of the Chair of MSAP, provided the total number of such observers does not exceed one-quarter total attendance. Staff and Trustees have observer status (do not score research proposals or contribute to quorum).
- 11.4.** National DEBRA CEOs providing funding for that round may attend the meeting as an observer.

APPENDIX 1

EB-ResNet mission and support for EB research

Mission: Translating successful research into patient benefit.

- EB-ResNet supports research to ensure that people with EB patients have access to effective therapies and treatments, and improved diagnostics in the near future.
- EB-ResNet is building collaboration between EB patient advocacy groups, researchers and industry partners to expedite research translation for clinical benefit.

DEBRA International's mission

DEBRA International's mission

- DI works on behalf of those affected by the skin blistering condition epidermolysis bullosa (EB).
- DI's vision is to ensure that people living with EB have access to the best quality support and medical care, and to drive the development of effective treatments and cures for EB.

DI Support for EB research

- DI's commitment to research addresses both short- and long-term goals:
 - DI supports translational research to get potential therapies developed for clinical use as efficiently as possible.
 - DI continues to support fundamental and novel-concept research - which may ultimately lead to better clinical management, diagnostic methods and therapies.
- DI's Research Priorities are established according to DI's stated mission, and in accordance with the increase in knowledge of EB through fundamental research, the development of technology, and opportunities for exploitation for the benefit of people with EB.
- DI states its research priorities in its Research Strategy document, and publicizes them via the website and in publications.
- DI's Research priorities are reviewed every three years, following DI's triennial consensus research conferences, and in response to input from DI's scientific and clinical advisers, including Medical & Scientific Advisory Panel, Translational Research Advisory Panel, and other DI advisory groups as may be created.
- DI maintains links with other funding bodies, and other national and international government bodies (including healthcare regulatory agencies) and NGOs working on behalf of people with rare diseases.
- DI maintains links, proactively and reactively, with the biopharma and healthcare industries, but does not enter agreements to endorse specific products.

APPENDIX 2

Scoring of research-grant applications: Notes for MSAP members and external peer-reviewers

External peer-reviewers (includes MSAP members asked to provide pre-meeting reviews of research-grant applications):

- You can provide detailed information on specific aspects within the reviewer's report form.
- Your scores will be used as an indication of your overall opinion of the grant application, in consideration of your report by MSAP.
- You are asked to provide 3 separate scores (whole numbers only on a scale of 0-10):
 - **Scientific merit and innovation**
 - **Feasibility and value for money**
 - **Ultimate benefit to patients with EB**, in either the short-term or longer-term (note that this would not exclude research into the fundamental biology or genetics of EB, if such knowledge is a pre-requisite to gaining an understanding necessary for eventual therapy or diagnostics development).

MSAP scoring of proposals at MSAP meeting:

- Only scores allocated at MSAP meetings, on completion of discussion of a grant application, will be used in the final scoring.
- At the MSAP meeting you will be asked to provide one score (on a scale of 0-100), combining consideration of the above 3 criteria.
- The average scores of MSAP members for each project will be used to make funding recommendations:

Projects scoring > average 70 are recommended as of **international standard and fundable**.

Projects <55 require major revision and should not be funded without revision and reassessment. These may be submitted to the next available grant round or managed locally as appropriate: any serious fault with research methodology raised by MSAP or DI is communicated back to researchers, and should be remedied before the research is funded.

Projects scoring 55-70, may be viewed as projects fundable if of importance to national DEBRAs (any serious fault with research methodology raised by MSAP or DI is communicated back to researchers, and should be remedied before the research is funded)*.

* Where a national member DEBRA has an overriding reason (e.g. building national EB-research capacity) for funding research considered by MSAP to be of 'national standard', but not 'international standard'. Research of national standard which is fundable in this way has usually failed to reach international standard because of lack of innovation or being less likely to have a major benefit on patient wellbeing.

Please follow this guidance in scoring:

MSAP meeting score (0-100)	Pre-meeting review score (0-10)	Interpreted as:
100	10	Perfect proposal in every way; highest global standard of innovative scientific investigation, essential to EB research, no changes required to proposed budget, personnel or methodology
90-99	9	Outstanding research proposal, possibly some minor suggestions for amendments to e.g. budget, timescales, personnel
80-89	8	Excellent research proposal, some minor suggestions for amendments to e.g. budget, timescales, personnel, methods or additional experiments
70-79	7	Very good research proposal, some suggestions for amendments to e.g. budget, timescales, personnel, methodology; may require clarifications or amendments to workplan to be submitted before grant can be offered.
60-69	6	Good proposal broadly but probably not fundable in current form : likely to need re-working with regard to aims, methods, budget, personnel, and timescale. Would need to be revised in line with MSAP/ DI recommendations and revisions agreed by DI.
50-59	5	Proposal not fundable as international standard owing to significant flaws in methodology, aims, budget, personnel, timescale, or lack of innovation, or targeting EB research priorities. Would need to be revised in line with MSAP/DI recommendations and revisions agreed by MSAP and DI.
40-49	4	Proposal not fundable owing to significant flaws in methodology, lack of innovation; questionable relevance to EB; inappropriate aims unlikely to benefit patients short or long-term. Discourage from resubmission.
0-39	0, 1, 2, 3	Proposal not fundable owing to major flaws probably in hypothesis or scientific reasoning; irrelevance to EB or misunderstanding of biology or clinical problems in EB; inappropriate methodology. Should not be resubmitted.

APPENDIX 3

The role of the Patient Representative (PR) on MSAP

1. The Patient Representative (PR) has the unique role of representing the interests of patients with any type of EB, and their families.
2. The purpose of the PR role is to bring this perspective into discussion and evaluation of research proposals and projects in the context of the DEBRA International Medical & Scientific Advisory Panel (MSAP).
3. The PR should have personal experience of EB, either as a patient, family member, or having represented the interests of EB patients and their families, and should be actively engaged with the EB patient and family community.
4. The PR does not need to have a science background, but must have sufficient knowledge and understanding of the key areas of EB research to grasp the broad concepts of a research proposal or a research report, and to consider the implications and applications of that research.
5. The PR should have a reasonable basic understanding of the genetic and molecular causes of EB, its inheritance, clinical and psychosocial consequences, and current standards of care, to allow them to have useful input, and to follow discussion of the research among a peer-group of academics and clinicians.
6. The PR will have a perspective which may be well understood by other members of MSAP, but is not their primary focus: it is essential that the PR is articulate, and can present concerns and questions clearly and confidently.
7. All written material and discussions are in English.
8. The PR must recognize that all materials (research proposals, reports, peer-review reports, and MSAP discussions and correspondence) are absolutely confidential and must not be discussed or otherwise communicated outwith their role as PR.
9. The PR does not have a formal vote at MSAP meetings where research proposals are evaluated for scientific quality, feasibility, contribution to body of knowledge, and budget.
10. The PR should be familiar with, understand, and embrace the mission of DEBRA International in its research priorities and support for patients with EB and their families.
11. The PR should be appointed by the DEBRA International Head of Research.
12. The PR should serve no longer than 4 years on the panel, but may serve longer by mutual agreement between DI, MSAP and the PR.