Dear Sir,

With this letter we, the ASAS (ASsessment in Ankylosing Spondylitis) working group, would like to express our interest in taking a lead in coordinating a critical appraisal of the science related to AS in answer to your request to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders in Federal Register, vol 66, no 98, May 21, 2001, notices.

The ASAS working group comprises epidemiologists, rheumatologists, and representatives of patient groups and industry with a special interest in the research of AS and related disorders. Many of them are opinion leaders in this field. The ASAS working group represents more than 20 countries. ASAS has started in 1995, organises regular meetings and workshops (at least twice a year), and conducts research, mainly in the field of outcome assessment in AS. As a result of these efforts core sets for the assessment of disease activity and outcome in various situations have been developed. In addition to this, response criteria based on a statistical data-driven approach have been proposed. At the moment, these response criteria are being tested against the “expert judgement” making use of a Delphi exercise. Publications in relation to the research performed, as well as a summary of the ongoing research agenda is attached to this letter. We would like to mention that Jennifer Anderson, Boston, has been deeply involved in the development of the ASAS set of responder criteria and that she could be of great value in participating at this process.

Taking into account the members of the ASAS working group and the scope of the research performed by this group, we would be happy to collaborate in the development of a guidance document including the critical appraisal that is needed for that purpose. We also would like to participate in a public meeting permitting to discuss selected relevant questions.
On behalf of all ASAS working group members (a list of the members is enclosed),

The steering committee,

Prof. N. Bellamy, Brisbane, Australia

Dr. A. Calin, Bath, UK

Prof. M. Dougados, Paris, France

Prof. D. van der Heijde, Maastricht, the Netherlands

Prof. A. Khan, Cleveland, USA

Prof. Sj. van der Linden, Maastricht, the Netherlands

On behalf of the Steering Committee,

Prof. D. van der Heijde
Department of Internal Medicine
Division of Rheumatology
University Hospital Maastricht
PO Box 5800
6202 AZ Maastricht
The Netherlands
Publications by ASAS


5. van der Heijde D, van der Linden S, Bellamy N, Calin A, Dougados M, Khan MA. Which domains should be included in a core set for endpoints in ankylosing spondylitis? Introduction to the ankylosing spondylitis module of OMERACT IV. J Rheumatol 1999;26:945-7.


Research agenda ASAS

- Delphi exercise to compare expert judgments with ASAS preliminary response criteria
- Performance of response criteria in trials with biological agents
- Additional value of CRP above ESR
- Severity of morning stiffness of the spine compared to duration of morning stiffness
- Various scoring methods of X-rays
- MRI of the spine as an outcome measure for disease activity and severity
- BASDAI
- BASMI
- Co-calibration of BASFI and Dougados FI
- Validation of QoL instruments in AS
<table>
<thead>
<tr>
<th>Name</th>
<th>Residence</th>
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<tbody>
<tr>
<td>Prof. A.O. Adebajo</td>
<td>Barnsley</td>
<td>United Kingdom</td>
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<td>Dr. B.L. van Albada</td>
<td>Oranjerwoud</td>
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<td>Prof. N. Bellamy</td>
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<td>Mrs. J. Bruckel</td>
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<td>Dr. R. Burgos Vargas</td>
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<td>Dr. A. Calin</td>
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<td>Prof. D. van der Heijde</td>
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<tr>
<td>Prof. H. Zeidler</td>
<td>Hannover</td>
<td>Germany</td>
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</tbody>
</table>
Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

Ewa Stanisławska-Biernat

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville
MD 20857
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Yours sincerely,

[Signature]
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Yours sincerely,

[Signature]

[Address]

706-233 KENNEDY STREET / WINNIPEG, MB CANADA R3C 3J5 /PHONE (204) 947-1766 /FACSIMILE (204) 947-1804
Dear Sir,

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Yours sincerely,

Muhammad A. Khan, M.D.
Professor of Medicine
Case Western Reserve University, Division of Rheumatology
2500 MetroHealth Drive
Cleveland, OH 44109
USA
Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

dr. A. Linssen
reumatoloog
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Yours sincerely,

Nils Feltelius
MD, PhD, Associate professor in Rheumatology
Department of Medicine, Karolinska Institute and
Division of Clinical Trials
Medical Products Agency
S-751 03 Uppsala
Sweden
July 23, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville
MD 20857

Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

John Darmawan, MD, PhD
Director, Seroja Rheumatic Center.
Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

Fergus J Rogers
Director
June 29, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20857

Dear Sir,

As a member of the ASAS working group, I would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Sincerely,

Jane Bruckel
Executive Director
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville
MD 20857

Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

I.E. van der Horst-Bruinsma, MD, PhD
Department of Rheumatology
Vrije Universiteit Medical Centre
PO Box 7057
1007 MB Amsterdam
The Netherlands
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville
MD 20857

Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

Marjatta Leirisalo-Repo, MD
Professor of Rheumatology
Helsinki University Central Hospital
Department of Medicine
Division of Rheumatology
PO BOX 263
FIN-00029 HUS
Finland
Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

Andrei Calin, MD, FRCP
Consultant Rheumatologist.
June 25, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5830 Fishers Lane, Room 1061
Rockville, MD 20857
USA

Dear Sir:

As a member of the ASAS working group, I would like to express my support of the initiative of this group in taking a lead in coordinating a critical appraisal of the science related to ankylosing spondylitis. This initiative specifically refers to the request of the FDA to assist in the development of guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

A.S. Russell, F.R.C.P.(C)

ASR/js
Dear Sir,

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Yours sincerely,

Prof. Dr. med. H. Zeidler
Dear Sir,

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Yours sincerely,

Dr. Shander Erdess, MD, PhD
Scientific Director
Institute of Rheumatology
Kashirskaya Street 34A
115522, Moscow, Russia
Tel/Fax: 7(095) 114-4486
Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville
MD 20857

Dear Sir,

With this letter I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,

[Signature]

UniversitätsSpital Zürich
Prof. Dr. med. B. A. Michel
Direktor Rheumaklinik
Gloriastrasse 25
CH-8091 Zürich
Dear Sir,

With this letter, I, being a member of the ASAS working group, would like to express my support to the initiative of the ASAS working group in taking a lead in coordinating a critical appraisal of the science related to AS. This initiative refers to the request of the FDA to assist in the development of a guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders.

Yours sincerely,
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   - Name: P DDS.鹅O Management Branch
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3. Your Internal Billing Reference:
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   - Dimensions: NA

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7. Special Handling:
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8. Payment:
   - Prepaid
   - Customer account number

9. Required Signature:
   - Signature
   - Date: 02/06/2007

10. Additional Information:
    - Origin Station ID: 8260 7240 2483
    - Destination Station ID: 0408