SOMETHING IS ROTTEN IN DENMARK

Analysis of the Social Network of Authors in Four Recent Articles on Autism, Mercury and Selected Childhood Vaccine Exposures and Assessment of the Role, Influence and Interests of the Statens Serum Institut in Issues of Vaccine Safety Studies

Safe Minds
May, 2004
SUMMARY (1)

Three recent studies based on data from a Danish patient registry have attempted to refute the link between mercury-containing vaccines and autism. These studies comprise the output of a deliberate and coordinated plan to attack the autism-mercury connection. Following behind a similar Danish registry analysis of the autism-MMR vaccine link, these three studies were all

- published in rapid succession in prestigious journals
- based on slightly different (but analytically non-comparable) views of the same event
- prepared by author groups with substantial connections and overlaps

These author groups comprise a social network with strong personal and institutional ties. These ties create a significant conflict of interest that was not reported in any of the journals. The entire author network has ties to a for-profit, Danish vaccine manufacturer: the Statens Serum Institut (SSI). SSI authors hold positions of substantial influence in the author network, while SSI occupies a central position of leadership in the network of participating institutions

- SSI directly employs over one-third (6 of 17) of the study authors
- SSI “houses the central unit of the Danish Epidemiology Science Centre”, the employer for the first authors of 2 of 3 studies, and for 7 of 17 of the authors (four of whom are not directly employed by SSI)
- SSI staff have co-authored at least six additional studies with two employees of the Danish National Centre for Register-based Research
- CDC employees and consultants make up the largest non-Danish group (3 of 17)

This collection of three articles, more appropriately viewed as a single networked initiative dominated by SSI, were therefore directly influenced by the financial interests of a manufacturer of final products (historically) and components (currently) for thimerosal-containing vaccines.
SUMMARY (2)

SSI is a for-profit, state-owned enterprise with roughly $120 million in annual revenue. They report income statement and balance sheet information, including measures of return on invested capital. Their research activities support their business interests.

The commercial interests of SSI are strongly tied to the success of their vaccine products and, especially to their exports outside Denmark:

- vaccines represent half of SSI’s revenues and over 80% of its profits
- vaccine exports appear highly profitable and represent SSI’s fastest growing business segment
- important export markets include the United States and the United Kingdom, home to active vaccine safety controversies

SSI has a direct financial interest in the autism-mercury controversy, with possible product liability due to their past production and revenue risk based on the demand for their intermediate products.

- SSI manufactured the (now discontinued) mono-component pertussis vaccine under investigation in the three studies
- SSI exports diphtheria and tetanus toxoid products used in thimerosal-containing vaccines still sold in the United States and the United Kingdom
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Four articles from Denmark have examined autism vaccine controversies. Three of these have recently addressed the autism-mercury connection.

The author network involved in preparing these studies is highly connected:
- most authors work in Denmark.
- many authors participated in more than one study and provide strong links across all four studies.
- a few key institutions provide the home for the majority of the network.
- Statens Serum Institut (SSI) employees play a central role in the network.

Most network participants either work directly for SSI or work for institutions with strong ties to SSI.
<table>
<thead>
<tr>
<th>Journal</th>
<th>Title</th>
<th>Authors</th>
<th>Reference</th>
</tr>
</thead>
</table>
AUTHORS BY COUNTRY

Note: Thicker line means authors have written two papers together
KEY AUTHOR AFFILIATIONS

Danish Epidemiology Science Centre (DESC)  
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Statens Serum Institut, Copenhagen, Denmark

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Anders Hviid, M. Sc.  
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Department of Medicine  
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Carsten B. Pedersen, M.Sc.

Centers for Disease Control and Prevention  
Atlanta GA, USA

Diane Simpson, M.D. Ph.D. (NIP)(1)  
Diana Schendel, Ph.D. (NCBDDD)(2)  
Paul Stehr-Green, Dr.P.H. M.P.H. (consultant)

(1)  National Immunization Program  
(2)  National Center on Birth Defect and Developmental Disabilities
# Measures of Author Centrality in the Network

## Degree Centrality

<table>
<thead>
<tr>
<th>Author</th>
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## Eigenvector Centrality

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</table>

1. High degree centrality means that author connects to many other nodes.
2. High betweenness centrality means others have to go through this author often to connect to others.
3. High closeness centrality means that the author is close to many others in the network.
4. High eigenvector centrality means that the author is connected to other authors who are well connected.
SEVEN CORE AUTHORS WITH HIGHEST SCORES FOR BEING AT THE CENTER OF THE NETWORK

- Madsen KM
- Lauritsen MB
- Pedersen CB
- Thorsen P
- Plesner AM
- Andersen PH
- Pedersen CB
- Stehr-Green P
- Tull P
- Stellfeld M
- Simpson D
- Hviid A
- Wohlfahrt J
- Melbye M

Note: Thicker line means authors have written two papers together.
FOUR CORE AUTHORS CONNECT THE KEY ORGANIZATIONS

Note: Thicker line means authors have written two papers together
LINKS BETWEEN KEY ORGANIZATIONS (1)
Statens Serum Institute (SSI), Department of Epidemiology Research and University of Aarhus Department of Epidemiology and Social Medicine

The Danish Epidemiology Science Centre was established in 1994 by the National Research Foundation. The Centre has 3 research units in Denmark located at Statens Serum Institut, Kommunehospitalet, Copenhagen and the University of Aarhus, respectively.

The board of the Centre is Jørn Olsen (Head), Mads Melbye, Thorkild IA Sørensen and Peter Aaby.

-Danish Epidemiology Science Center, http://www.epidemiology.dk/

The Department [of Epidemiology Research at SSI] furthermore houses the central unit of the Danish Epidemiology Science Centre, which was established as a network collaboration with two other institutions in Denmark, Department of Epidemiology and Social Medicine, Aarhus University, and Institute of Preventive Medicine, Copenhagen Hospital Corporation.

-Statens Serum Institut, Department of Epidemiology Research

LINKS BETWEEN KEY ORGANIZATIONS (2)
Department of Epidemiology and Social Medicine, University of Aarhus and
National Centre for Registry-based Research, University of Aarhus

Weekly gatherings

Furthermore, the [National] Centre [for Register-based Research] is involved in the seminars held every week at the Department of Epidemiology and Social Medicine, Aarhus University. The seminars take place every Friday morning at 9.00 in Building 261, 'Lunch room', at the ground floor.


University of Aarhus research centers sponsored by the Danish National Research Foundation

During the past year the University of Aarhus has been host to the following centres, which are all operating on five-year grants from the Danish National Research Foundation. The Danish Epidemiology Science Centre was established in 1994 with a grant from the Danish National Research Foundation. The Centre has research sections at the University of Aarhus, the Institute of Preventative Medicine in Copenhagen, Statens Serum Institut (the National Central Laboratory of the Danish Health System) and in Guinea Bissau. Head of Centre: Professor Jørn Olsen, PhD

The National Centre for Register-based Research opened on 1 September 2000 within the Faculty of Social Sciences at the University of Aarhus, occupying newly-renovated premises in the old Sahva Building at the former Orthopaedic Hospital. The Centre has a grant from the Danish National Research Foundation to finance its first five years of operation. After that, if the Centre is a success, it will be integrated into the structure of the University of Aarhus in some form or another. Head of Centre: Professor Preben Bo Mortensen, dr.med

LINKS BETWEEN KEY ORGANIZATIONS (3)
Statens Serum Institut (SSI), Department of Epidemiology Research and National Centre for Registry-based Research (NCRR), University of Aarhus

Six publications (excluding autism studies), in which autism principals from SSI and NCRR were co-authors

   Mortensen PB, (NCRR) Pedersen CB (NCRR), Westergaard T (SSI), Wohlfahrt J (SSI), Ewald H, Mors O, Andersen PK, Melbye M (SSI)

   Valeur-Jensen AK, Pedersen CB (NCRR), Westergaard T (SSI), Jensen IP, Lebech M, Andersen PK, Aaby P (SSI), Pedersen BN, Melbye M.

   Westergaard T (SSI), Mortensen PB (NCRR), Pedersen CB (NCRR), Wohlfahrt J (SSI), Melbye M (SSI).

   Nielsen NM (SSI), Wohlfahrt J (SSI), Aaby P (SSI), Hjalgrim H (SSI), Pedersen CB (NCRR), Askgaard DS, Melbye M (SSI).

   Torrey EF, Mortensen PB (NCRR), Pedersen CB (NCRR), Wohlfahrt J (SSI), Melbye M. (SSI)

   Westergaard T (SSI), Mortensen PB (NCRR), Pedersen CB (NCRR), Wohlfahrt J (SSI), Melbye M (SSI)
INSTITUTIONAL TIES UNDERLIE AUTHOR NETWORK

Statens Serum Institut
(Drs. Mads Melbye
and Michael Stellfeld)

Danish Epidemiology
Science Centre

Extensive cross-authorship
involving autism principals

Weekly meetings and
common funding source

University of Aarhus
Department of Epidemiology
and Social Medicine
(Professor Jorn Olsen)

National Centre for
Register-based Research
(Professor Preben-Bo Mortensen)
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THE COMMERCIAL INTERESTS OF STATENS SERUM INSTITUT

Key leaders of the author network occupy leadership positions in SSI

The vaccine division plays a critical role in the financial performance of the company

- half of revenues and over 80% of profits
- vaccine exports are the fastest growing and (possibly) most profitable segment of SSI’s business
- mercury-containing products play a significant role in the financial outlook for SSI’s vaccine export business
- SSI provides vaccine ingredients for mercury-containing vaccines currently in use in the United States and the United Kingdom

SSI has a direct financial stake in assessments of vaccine safety

- revenues could decline sharply if DT and TT products are recalled or discontinued
- product liability issues could arise if past vaccine production is linked to autism
STATENS SERUM INSTITUT ORGANIZATION CHART

Source: Statens Serum Institut web-site, http://www.serum.dk/sw1482.asp
STATENS SERUM INSTITUT REVENUE GROWTH DRIVEN BY VACCINES AND (MOSTLY VACCINE) EXPORTS

Note: *Exports includes all products, but 88% of 2002 export sales came from vaccines
Source: Statens Serum Institut, 2002 Annual Report
OVER 80% OF STATENS SERUM INSTITUT’S 2002 PROFIT CAME FROM VACCINES, INCLUDING SIGNIFICANT EXPORT SALES

Source: Statens Serum Institut, 2002 Annual Report
### Vaccine production departments
- **Viral vaccine department** (42 employees, single unit)
  - Tetanus unit
  - Diphtheria unit
  - Media unit
- **Bacterial vaccine department** (30 employees, 4 units)
  - Tetanus unit
  - Diphtheria unit
  - Media unit
  - Toxoid development unit
- **BCG and sterile filling and formulation department** (55 employees, 3 units)
  - Sterile unit
  - BCG unit
  - Packing unit

### Vaccine products
- **Injected polio vaccine (IPV)**
- **Tetanus toxoid**
- **Diphtheria toxoid**
- **Growth and culture media, buffers for virus and bacteria cultivation**
- **Toxoid development**
- **BCG vaccine for tuberculosis**
- **BCG culture for bladder cancer**
- **Preparation and packaging for all SSI vaccine products and exports**

### Customers and markets
- **Danish government for domestic IPV program**
- **Working on U.S. FDA approval**
- **Denmark, U.S. and Europe**
- **Internal**
- **Danish government and “export trade”**

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Source: Statens Serum Institut web site, [http://www.serum.dk/sw1482.asp](http://www.serum.dk/sw1482.asp)
STATENS SERUM INSTITUT PROVIDES COMPONENTS FOR DT, TT AND DTaP VACCINES IN THE UNITED STATES

Reference Numbers: 95-1530, 95-1531 and 95-1532

Ms. Brigitte W. Knudsen
Statens Seruminstitut
S. Artillerivej
DK-2300 Copenhagen S
DENMARK

Dear Ms. Knudsen:

This letter hereby issues Department of Health and Human Services Biologics License No. 1255 to Statens Seruminstitut, Copenhagen, Denmark, in accordance with the provisions of Section 351(a) of the Public Health Service Act as amended November 21, 1997 (FDAMA; Public Law 105-115), controlling the manufacture and sale of biological products. This license authorizes you to manufacture and import into this country to ship for sale, barter, or exchange those products for which your company has demonstrated compliance with establishment and product standards.

Under this license you are authorized to manufacture the products Tetanus Toxoid Concentrate (For Further Manufacturing Use) and Diphtheria Toxoid Concentrate (For Further Manufacturing Use) to be shipped to North American Vaccine, Inc., in a shared manufacturing arrangement for the manufacture of Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed (DTaP).

JUL 28 1998
The 1st International Reference Reagent for TETANUS TOXOID FOR FLOCCULATION TEST
Code: TEFT
(Version 02)

1. INTRODUCTION

This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. With effect from 1st July 1997, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

The 1st International Reference Reagent for DIPHTHERIA TOXOID FOR FLOCCULATION TEST
Code: DIFT
(Version 02)

1. INTRODUCTION

This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. With effect from 1st July 1997, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

The package insert from SSI is attached.
RISKS

Vaccines
As a biological production, vaccine production, the main pillar in the development of revenue, is sensitive. For example, cultivation problems can occur as a consequence of quite small changes in the cultivation conditions. Some problems often emerge late in the production process, so rejects include not only raw materials but also the supplies and the work input.

Insurance
The Institute’s product liability insurance is expected to lead to a significant increase in expenses the coming years.

Source: Statens Serum Institut, 2002 Annual Report
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CONCLUSION

The recent series of articles on mercury and autism and Denmark were conducted and sponsored by a single network of authors.

Those authors were tied, either indirectly or as employees, to a for-profit vaccine manufacturer (SSI) with a direct financial interest in the outcome of the analysis. Their motivations as investigators were closely tied to the products they were investigating. They have a clear conflict of interest.

Statens Serum Institut relies heavily on its vaccine products for revenue, growth and profitability. The growth and profitability, in particular, of its export vaccine business provides strong incentives for SSI to build ties with public health officials and manufacturing partners in the United States and United Kingdom. SSI has a clear and strong interest in the policy debates surrounding the autism-mercury controversy. They cannot be considered an objective party.

SSI has a direct financial interest in the assessment of past mercury-containing vaccine safety issues and the future viability of mercury-containing products. Their participation in any analysis directly compromises the investigation. They should be excluded from further work in vaccine safety assessment.