

## FULL ARTICLE

# "Sinning against Science Itself": Adolf Friedrich Nolde's 1799 Code of Good Research Practice

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**In 1799, Adolf Friedrich Nolde, a German physician and academician, wrote a set of eight rules for the study and evaluation of drugs. His eighth rule focuses on research misconduct and is an early warning of the corruption that such practices can cause in the scientific literature. In this paper, we offer the first English translation of Nolde's rules and evaluate their significance, especially that of the eighth rule, in modern-day practice.**

**Key words:** Research misconduct, Ethics, Nolde, Code, Rules, Pharmacology

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## INTRODUCTION

Today, the name Adolf Friedrich Nolde is virtually unknown, even in the medical historians' circles. A young German professor of medicine and midwifery from the late eighteenth and early nineteenth centuries, this man, while mourned and eulogized at the time of his early death, has been quickly forgotten.

However, Nolde deserves to be remembered, and his work merits closer examination, especially because of his writings in the final years of the eighteenth century and his focus on the development of a scientific foundation for the study of drug treatments and the development of research ethics.<sup>1</sup>

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This work remains largely unknown partly because it has never been translated from the original German, and, despite some mention in the German literature,<sup>2</sup> it has not been critiqued. In this paper, we present the first English translation of Nolde's rules and focus on the eighth rule, which offers a warning against research misconduct and has as much relevance today as when it was written more than 200 years ago.

## His life

There is no contemporary or modern biography of Nolde that goes beyond the status of a simple obituary, and there seems not to be a single extant likeness of him in any of the universities in which he worked. We can, however, piece together his adult life story from a range of sources, but it is regrettably short and punctuated with tragedy.

Adolf Friedrich Nolde was born in Neustrelitz in northeast Germany in 1764. He studied medicine in Göttingen and Berlin and graduated in 1788. He returned to his birthplace to enter private practice, but, the following year, he moved to Rostock where he entered the University's Medical Faculty. He rose quickly and was appointed as Professor Extraordinary in 1790, Professor of Midwifery in 1794, and State Physician in 1797.<sup>3</sup>

His first marriage was in 1791 to Anna Dorothea Elisabeth Becker, the daughter of a Court Physician and Privy Counselor.<sup>4</sup> In 1801, she accompanied Nolde on a study trip to Italy. While in Rome in 1802, both contracted "nervous fevers." Nolde recovered, but his wife died.<sup>4,5</sup>

Widowed, he returned to Rostock in the autumn of 1803 and resumed work. In 1806 he was appointed as Professor of Midwifery at the Collegium Medico-chirurgicum in Brunswick and was entrusted with the Direction of the local Maternity Hospital. In addition, he became a Court Physician to the Duke of Brunswick. The same year, he remarried; his second wife was Friedrika Taddel, the daughter of a Court Counselor in Rostock, but Nolde would have no children.<sup>4</sup>

Regrettably, shortly thereafter, his patron the Duke of Brunswick (Braunschweig) died, and Nolde was severely affected by this reversal of fortunes and the political upheavals that ensued.

In May 1810, in an attempt to re-enter academic circles and improve his income, he moved to the University of Halle where he took the posts recently vacated by Johann Chris-

tian Reil, who had moved to be the Dean of the new medical faculty in Berlin. In Halle, he became Professor of Therapy, Director of the Academic Clinic, and the City's Medical Officer.

Throughout 1813 there was a typhus epidemic in Germany. It has been proposed that the epidemic may have been carried to Germany by returning soldiers from Napoleon's abortive 1812 campaign in Russia. Approximately 10% of the German population were infected, and of these, 10% (some 250,000) died.<sup>6</sup> Nolde was one among these; he contracted the disease and died in Halle on September 2, 1813, at the age of 49 years.

His premature death was a great shock to his academic colleagues, and it is a mark of the high regard in which he was held that he was given a grand and solemn funeral. He was accorded the singular honor of being laid to rest next to the body of the celebrated German Physician and Chemist Friedrich Hoffmann in the funeral vault of the University of Halle's Medical Faculty.<sup>4</sup>

### Nolde's rules

In his treatise, *Erinnerung an einige zur kritischen Würdigung der Arzneimitteln sehr nothwendige Bedingungen* [Reminder of some of the necessary conditions for the critical appraisal of a drug], published in 1799, Nolde defines and enumerates a set of eight rules for the conduct of pharmacological research (Table 1).

In the first seven of these rules, Nolde highlights the need for the study of high-quality and "genuine and unadulterated" drugs that are "prescribed in an appropriate manner." He recognizes that patients with well-characterized diseases should be studied and that any evaluation of new and untested drugs should be done "with the greatest caution." He emphasizes the need "to observe precisely the changes, which are induced by the application of a drug, and investigate properly whether they are caused by it or might be due to other precipitating factors" and "to repeat our experiments frequently under

similar and probably occasionally also under dissimilar conditions."<sup>1</sup>

It is his eighth rule, however, that merits the closest examination, for here he looks at the issue of research misconduct and the impact it may have on both scientific endeavor and patients' well-being.

He summarizes this rule as follows:

*"Rule 8. When announcing a new drug or recommending a known drug nothing at all should be omitted about anything that could have an influence on the correct assessment of the drug, and it would be shameful if observations were to be fabricated or distorted at the expense of the truth."*<sup>1</sup>

### Research misconduct

Nolde justifies the inclusion of such a rule by noting that, "unfortunately one sees many a result which has been recorded untruthfully," and goes on to state that, "not everything which physicians publish under the promising titles of 'Observations and Experiences' can be taken at face value."<sup>1</sup> What might be seen as very much a twenty-first-century problem appears to have been a well-recognized phenomenon even in the eighteenth century.

He describes instances of fabrication, where results are simply made up and then published, as well as instances of falsification, where results are willfully manipulated to tell a different story. In both, he expresses his concern that, "the public can be deceived in this way."<sup>1</sup> Moreover, he admonishes those whom he believes have corrupted the scientific literature:

*"Such actions are of course extremely unworthy of any honourable man and should rightly bring disgrace upon him. Not only does he deceive the reading physicians in this way and shamefully betray the time and effort invested by them with the best of intentions, but he is also sinning against science itself by wilfully corrupting the degree of certainty of which science is capable and acting irresponsibly."*

**Table 1:** Nolde's eight rules

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- 1 The remedies we apply in order to draw certain conclusions from their effects on diseases have to be of the highest quality, and they must be genuine and unadulterated.
  - 2 The drugs, which we investigate and determine with regard to their effects on diseases, have to be prescribed in an appropriate manner.
  - 3 When we try to determine by experiments the effect of a remedy on certain disease conditions, we have to investigate the course of the disease and its present nature with the utmost precision prior to the application of the drug.
  - 4 One should not try new drugs as long as one can rely on known and tested ones, and one should apply all new drugs with the greatest caution.
  - 5 In order to properly describe the effects of a drug under investigation, one has to know in particular which patients and which accidental courses of disease may produce certain results.
  - 6 We have to observe precisely the changes that are induced by the application of a drug and investigate properly whether they are caused by it or might be due to other precipitating factors.
  - 7 In order to develop the best possible understanding of the effects of a drug, we have to repeat our experiments frequently under similar and probably occasionally also under dissimilar conditions.
  - 8 When announcing a new drug or recommending a known drug, nothing at all should be omitted about anything that could have an influence on the correct assessment of the drug, and it would be shameful if observations were to be fabricated or distorted at the expense of the truth.
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*... toward the public who entrust their health and lives to their physicians. Anyone who dares to misrepresent the truth so deliberately should consider carefully the unpredictable consequences of his actions and look to his conscience!"<sup>1</sup>*

Nolde asks for a comprehensive approach to scientific reporting, but recognizes that this is a more difficult path:

*"Whoever has the will and resolve to present really instructive observations to the medical public will undoubtedly have to apply himself much more diligently than one who cares not what he writes to the world."<sup>1</sup>*

He also notes the difficulty this may present to the reader, but rejects the idea that this is an unnecessary burden:

*"I reject the criticism that the length and detail of such comprehensive reporting would bore and tire the reader. Anyone who, as a critic or a prospective physician seeking guidance, turns to such observations does not do so for amusement as in reading a novel. . . . The physician, if he so wills and has the ability to do so, can report his observations so that they read well and easily despite their necessary thoroughness. It is not the deluge of words or the number of pages that give a report its comprehensiveness, but rather the complete and accurate reporting of everything, which is relevant without falling into the trap of long-winded, tiresome verbosity. As regards the time a physician spends reading such reports of observations he would have much less cause for regret if, in a day, he read two or three well-written reports than if he read hundreds which were of little use."<sup>1</sup>*

He also recognizes the importance of education stating:

*". . . it would be very desirable if it were very strongly impressed on young physicians at university that their duty was to remain loyal to the truth in all circumstances and that plying their trade in silence would be preferable to doing so with lies and deceit."<sup>1</sup>*

Nolde concludes:

*"Only when we know this relationship exactly and that the tests which produced the data were undertaken with all practical care, intelligence, diligence and attention, are we able to obtain the information and the degree of certainty needed in order to judge the value or worthlessness of a drug. Truth is always better than deception and definite certainty preferable to precarious uncertainty."<sup>1</sup>*

Regarding the research misconduct that he recognizes as toxic to scientific endeavor and the practice of medicine, he recommends that it be exposed and expunged:

*". . . all corner-cutting, fabrications and deceptions of the 'literary' physicians, produced in their thousands, should be*

*treated with the greatest contempt as soon as they are recognized as such and deserve no better than eternal oblivion."<sup>1</sup>*

## DISCUSSION

Despite Nolde's relatively short professional life, his work, particularly in highlighting the importance, consequences, and prevention of research misconduct, deserves greater attention.

Working in the late eighteenth century, Nolde was part of the medical and scientific enlightenment that recognized the deficiencies of a past reliant on folklore and anecdotes to inform medical practices. He and many of his contemporaries realized that good practice had to be founded on experience and furthermore that that experience should be gathered and reported in a rigorous way.

Writing specifically about the evaluation of new drug therapies, Nolde enumerated a series of key principles or rules that he proposed must be followed for such assessments to be valid. What his rules cover are a number of the key aspects of the scientific method and would be readily recognizable to a modern-day clinical pharmacologist. In his discussion of these rules, he highlights the value of experience over speculation, and asks the physician to:

*"never lose sight of the elements which are essential for this endeavour so that his information does not do more harm than good! I feel this request is of all the more interest in our times when, despite all the desires to perfect our science, physicians often depart from the path of pure experience and seem to want to amuse the public with hypotheses and principles which do not always flow from the pure spring of experience."<sup>1</sup>*

But, in addition to these principles of practice, Nolde felt the need to emphasize the ethical aspects of research practice and reporting.

Today, we are acutely aware of the importance of research misconduct, and major efforts are being made to expose and root out such practices.<sup>7,8</sup> We understand how the fabrication and falsification of research data and their publication can fatally undermine modern medicine, but so did Nolde, more than 200 years ago. Not only did he recognize the problem, he also understood the implications of a corrupt scientific literature and its impact on patient care. He also realized that education of junior practitioners and researchers is key to both solving the problem and making the practice completely professionally unacceptable.

Nolde was not alone in attempting to place the evaluation of new drug therapies on a firmer scientific footing. His exact contemporary, Johann Christian Reil, another German academic physician, also published on this topic and indeed many of his principles and rules are similar to those of Nolde.<sup>9-11</sup> But, it was Nolde who chose to concentrate a

significant part of his treatise on the issue of research misconduct and false reporting of research findings.

Nolde's contribution not only is of interest for historical curiosity but is also a potent reminder that the challenges of clinical research are not new. The problems we face today are similar to those that troubled the minds of our forefathers. We are concerned with the quality of clinical research and its integrity and, at times, even its veracity. If we are looking for solutions, we might do worse than to consider those put forward by thinkers such as Nolde. Recognition of the problem, a public refusal to accept such a state of affairs, and then ensuring that junior staff are properly educated were Nolde's solutions. These are also increasingly the modern solutions to our problem of misconduct and fraud in scientific research.

### CONFLICT OF INTEREST STATEMENT

The Authors declare that there is no conflict of interest.

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