A brief history of European harmonization of disinfectant testing – a Dutch view

Die europäische Harmonisierung der Desinfektionsmittel – Testverfahren aus der Sicht eines Niederländers

Abstract

Since 1970 we know in Europe that, by engaging in intensive dialog and constructive cooperation it is possible to achieve a generally acceptable test procedure, despite the many divergent approaches taken by the different countries. When in 1966 I began my career as a microbiologist, different procedures were used in all countries to test the efficacy of disinfectants. The results of such tests did not at all lend themselves to comparison.

One of the most important requirements to be addressed to a future, generally acceptable procedure was naturally that the results should be reproducible. To that effect, it was necessary to standardize all aspects of the test since even the slightest discrepancy could give rise to markedly different results. On the other hand, each specified detail had to be scientifically corroborated to prove acceptable to all parties. 1990 marked a major breakthrough towards harmonization of European disinfection test procedures with the founding of the “Chemical Disinfection and Antiseptics” (TC 216) working group within the framework of the “European Committee for Standardization (CEN). This served as a basis for Phase 1 (basic evaluation of the disinfectant effect or suspension tests under different conditions) and Phase 2 tests (tests on different surfaces under practice-oriented conditions). The quantitative principle is now valid for both phases. Major investments were needed to bring about European harmonization. We Dutch, in particular, are well known for having our own opinions. But we, too, continued to engage in discussions and collaborations until we reached a consensus and learned to respect each other and even to become friends in some cases.

Today, harmonization endeavors extend well beyond Europe: with its biocide program, the OECD pesticides working group is working towards the development of a global test procedure for disinfectants. So we have not, by any means, reached the end of the road: there is still much to be accomplished by our successors: I am confident that we shall succeed, because no one – neither the manufacturers nor the authorities – can negate the knowledge base on which the European standards are founded.

Zusammenfassung

Seit 1970 beweisen wir in Europa, dass es möglich ist, durch einen intensiven Dialog und konstruktive Zusammenarbeit aus vielen nationalen Vorgehensweisen zu einem allgemein akzeptierten Testverfahren zu kommen. Als ich 1966 meine Arbeit als Mikrobiologe begann, wurden die Desinfektionsmittel in jedem Land mit unterschiedlichen Testverfahren auf ihre Wirksamkeit getestet. Die Ergebnisse der Tests waren in keiner Weise vergleichbar.

Eine der wichtigsten Forderungen an ein zukünftiges, allgemein akzeptiertes Verfahren war natürlich, dass die Ergebnisse stabil bleiben sollten bei Test – Wiederholungen. Dazu war es notwendig, das Testverfahren in jedem Detail zu standardisieren. Kleinste Abweichungen konnten zu

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deutlich anderen Ergebnissen führen. Jedes festgelegte Detail musste andererseits wissenschaftlich begründet sein, wenn alle es akzeptieren sollten. Ein großer Durchbruch für die europäische Abgleichung der Desinfektionsmitteltestung war 1990 die Gründung der Arbeitsgruppe „Chemische Desinfektion und Antiseptica" (TC 216) im Rahmen des „European Committee for Standardization (CEN)“. Jetzt entstanden Tests für die Phase 1 (grundsätzliche Beurteilung der desinfizierenden Wirkung bzw. Suspensionstests unter unterschiedlichen Bedingungen) und Phase 2 (Test auf unterschiedlichen Oberflächen unter praxisnahen Bedingungen). Das quantitative Prinzip ist nun für beide Phasen gültig. Der Aufwand für die europäische Einigung war groß. Gerade wir Holländer sind ja bekannt dafür, ihre eigene Meinung zu haben. Aber auch wir haben solange diskutiert, so lange zusammen gearbeitet, bis wir zusammen gefunden haben, gelernt haben, uns gegenseitig zu respektieren, zum Teil sogar Freunde geworden sind.

Heute gehen die Einigungsversuche weit über Europa hinaus: die Arbeitsgruppe für Pestizide der OECD arbeitet im Zusammenhang mit ihren Biozid-Programm daran, ein global einheitliches Testverfahren für Desinfektionsmittel zu erreichen. Wir sind also noch lange nicht am Ende angelangt, viel bleibt für unsere Nachfolger noch zu tun. Ich bin zuversichtlich, dass das gelingen wird, denn niemand – weder die Hersteller noch die Behörden – können das Wissen negieren, auf dem die europäischen Standards beruhen.

Development of quantitative suspension tests from 1970 onwards

When I started my career at the National Institute of Health in the Netherlands in 1966 my task was research and assessment of antimicrobial agents, i.e. antibiotics and disinfectants. Quantitative testing of disinfectants was initiated in our laboratory to evaluate new disinfectant products under the Pesticide Act, published in 1963. Our Standard Suspension Test (SST) was based on the so called 5-5-5 test, introduced by Mossel for the rapid evaluation of disinfectants intended for use in food processing plants [1].

At that time a variety of test methods was in use in the different countries, most of them qualitative (end point) tests. That was the reason why in 1970 and 1972 the first and second International Colloquium about the Evaluation of Disinfectants In Europe were organized in Hamburg [2], [3]. My memory of the latter meeting - organized by the European Committee under the auspices of the Rudolf Schülke Foundation - is still vivid since there I met for the first time the colleagues that played a major role in the harmonization efforts to come.

The necessity of harmonization was illustrated by Reybrouck, who compared the four main suspension tests in use at that time, i.e. the qualitative use-dilution test of the A.O.A.C. (USA), the qualitative suspension test of the German Society for Hygiene and Microbiology, the quantitative Dutch Standard Suspension Test and a qualitative capacity test (‘Kelsey-Sikes test’) in use in the United Kingdom. The main conclusion from this comparison was that the methods differ to such an extent that ‘there is no way of establishing a comparison between the results of the four methods with a view of setting up a conversion table. Each disinfectant testing technique has its own characteristics [4].

In the mean time the French Normalization Institute (AFNOR) had adopted the principle of quantitative testing [5]. Moreover Reybrouck and Werner, on behalf of the European Committee, expressed their preference for a quantitative suspension test on the basis of their comparative studies and the experience in France and the Netherlands [6].

An important issue was and still is the repeatability and reproducibility of these tests. That is why we carried out, in the mid seventies, a collaborative study with the SST in which 10 laboratories participated, including the laboratories of 5 major manufacturers of disinfectants: Akzo Chemie, Benckiser, Th. Goldschmidt, Schülke & Mayr and Unilever Research. The results indicated that within the range of measurable M.E. (microbicidal effect) values many replications are necessary to obtain a manageable precision, and that improvement could probably be obtained by a more rigorous standardization of the method [7].

A logical further step in this respect was the decision taken during a meeting of the extended European Committee in Mainz [8] to carry out an international collaborative study with the objective to arrive at an internationally accepted quantitative suspension test (QST); the results were published in 1979 [9]. However, this test procedure never reached the status of internationally accepted QST, since the European Committee stopped its activities in 1978.

A further opportunity on the track to European harmonization occurred by the initiative from the Netherlands to organize a collaborative study within the framework of
the Council of Europe, again with the objective to design a reference method acceptable for all member countries. A more standardized version of the SST was used in this ring trial, in which again 10 laboratories participated. The results were not much better than our first collaborative study with the SST. A survey carried out after completion of the study revealed that a major source of variation was probably the way the use dilutions of the disinfectants were prepared; so in consultation with a selection of international experts the method was redrafted and more rigorously standardized and finally published as the European Suspension Test (EST) under the auspices of the Council of Europe in 1987 [10]. Strictly the method was only intended for disinfectants in the food industry, but was potentially also useful for the medical and veterinary sector.

Development of carrier tests

From the start of designing suspension tests it was generally recognized that exposing micro-organisms in suspension to an excess of disinfectants is far from the situation in real practice and of limited value in predicting the effectiveness of these products under practical conditions. For this reason many laboratory procedures have been developed mimicking the latter conditions. These methods have in common that the test organisms are dried on a carrier - usually glass, tiles or stainless steel - and subsequently exposed to a small volume of the disinfectant; after exposure the surviving germs are recovered and counted by standard plate counting procedures. One of the main differences between these methods is the way of recovery of the germs from the carriers e.g. by rinsing, swabbing or impression. In 1977 Borneff and co-workers published a series of articles on this subject in the Zbl. Bakt. Hyg., among others a comprehensive literature survey [11].

In our view the, at that time, preferred German impression method with Rodac plates was more laborious and less reliable than the rinsing technique as described in the Dutch quantitative carrier test (QCT) [12]. The latter technique was also preferred by Reybrouck after extensive comparative testing [13]. He showed that the differences between the various methods - with regard to carrier types, inoculum preparation, organic load, exposure times, recovery procedure and interpretation criteria - may result in significant differences in the outcome (reduction factors) of the test.

A major breakthrough: The CEN/TC 216 experience

In spite of all the aforementioned efforts no harmonization or mutual acceptance of the different national test methods was reached and manufacturers, wanting to register their products in the different European countries, were faced with high costs for efficacy testing according to each national requirement. Early in 1989 I was asked by representatives of our government and the Dutch Normalisation Institute to give my view on a proposal by the European Committee for Standardization (CEN) to start a TC on disinfectant testing. The initiative for this project was taken by the British Standardization Institute (BSI) in September 1988, through application of a Form A (CEN N 676) asking to start standardization work on disinfectants for agricultural, veterinary, food and industrial applications, followed by additional proposals of AFNOR and SNV to include antiseptics and medical applications. On 18 September 1989 a meeting took place in Brussels of an ad hoc group on disinfectants and antiseptics, in which CEN and the normalisation institutes of the UK, France, Germany and Switzerland participated. During that meeting it was decided to create a TC entitled ‘Chemical Disinfectants and Antiseptics’, and the secretariats of the TC and its working groups (medical, veterinary and food/industrial respectively) were allocated. In the same month a European symposium took place in Fougères (Fr.) under the auspices of the French ministries covering those fields, where representatives of many countries summarized and discussed the different national test methods and regulatory procedures [14]. In the mean time I had warmly subscribed to the CEN initiatives and was asked to represent the government/National Institute of Health of the Netherlands at the first and founding meeting of the new TC 216, on 25/26 April 1990.

During that first meeting Prof. Reber was chosen unanimously as chairman. One of the resolutions of this first meeting pertained to the scope being: ‘Standardization of the terminology, requirements, test methods including potential efficacy under in use conditions, recommendations for use and labelling in the whole field of chemical disinfectants and antiseptics’. The aim was to design a set of test methods that should be adopted on a European level, taking into account the experience in this field obtained in the past decades in the different countries of the European Community.

TC 216 embarked on a programme comprising respectively so called phase 1 tests, i.e. preliminary suspension tests to verify whether a product deserves the qualification ‘disinfectant’, phase 2 tests covering suspension tests under a variety of test conditions (step 1) and tests on surfaces that mimic practical conditions (step 2). We decided to abstain from designing tests under real practical conditions (phase 3 tests), since these conditions may vary considerably and are hard to standardize. Close to practice however are the tests for hygienic and surgical hand disinfection that were developed based on the methodology designed by Rotter and co-workers in Vienna in the 1970-ies [15].

From the start the committee adopted the principle of quantitative testing for all phases. In numerous sessions of the different working groups the details of the draft methods were discussed. Although the process was time
Development of a European surface test

In 1991 an expert group from CEN/TC216 – so called Surface Test Group (STG), that I was privileged to chair, was asked to develop a well standardized European surface test method. After lengthy discussions we concluded that the primary goal of such a test should be to obtain quantitative information about the efficacy (killing potential) of disinfectants on bacteria attached to hard surfaces, keeping in mind that information about killing of bacteria that are dispensed in a disinfectant solution, is obtained in the suspension tests, usually carried out prior to surface testing.

In 1993 the first draft of a ‘basic’ surface test was designed. Small circular stainless steel surfaces (2 cm diameter) were chosen as carriers, as proposed by Dr. Sally Bloomfield (UK). The first results obtained in a collaborative study with this draft European surface test were published in 1995 [16]. Subsequently the principles of this methodology were used by the different WG’s to design their own surface tests, among others a particular variant for instrument disinfectants.

Other special Task Groups

The principle of creating task groups of experts for developing a basic methodology for a particular field appeared to be fruitful and was also applied for test procedures with mycobacteria, spores and viruses; those groups – respectively chaired by Dr. Orefici (It.), Dr. Böhm (Ge.) and Dr. Thraenhart (Ge.) – reported to the so called Horizontal Working Group (HWG). Once accepted the other WG’s (medical, veterinary, institutional) were supposed to adopt and include these principles in their own test methods that could be modified for special purposes with regard to test strains, contact times, interfering substances etc.

Main points of discussion

It goes without saying that this brief history doesn’t allow presentation or discussion of technical details. In retrospect the main issues of discussion were and still are (i) the reliability, i.e. the repeatability and reproducibility of the tests, (ii) the relevance of the different suspension- and carrier tests with regard to finding the proper concentrations for practical use, (iii) the relation between the different tests with respect to minimum requirements for the respective fields of application.

Ad (i): The first topic was approached by organizing ring trials with the different CEN Standards. The first one, so called Andistand project with the basic (phase 1) suspension test, was for a me a special scientific and social experience, with frequent meetings in Paris where we discussed the results of the ring trial with the statistician; main contributors were Dr. Andrée Cremieux and Dr. Hans-Joachim Rödger.

The findings indicated that the reproducibility and reliability of the test were similar to our earlier findings with the Dutch SST; the implication is that to obtain a reasonable precision the test has to be repeated many times, for instance to get a 90% probability that the ‘real’ M.E. value will not differ more than 1 log from the measured M.E. value, the test has to be repeated about 8 times. Similar findings were obtained in a second major ring trial project (leaders Drs. Rödger and Gebel) with tests for instrument disinfectants. Obviously a requirement to repeat each test many times will render disinfectant testing for manufacturers unacceptably expensive. A reasonable compromise still has to be decided upon.

I want to emphasize that the organization and design of these ring tests was relatively difficult and time consuming and required a lot of idealism form the participants, in particular while funding was usually limited.

Ad (ii): The second topic is as old as disinfectant testing itself. Although it is generally recognized that suspension tests are relatively simple tests in which contact between micro-organisms and disinfectant is optimal and far away from practical conditions, use dilutions are often based on the concentrations that pass such a test; the usual requirement is that these concentrations should induce at least 5 log reduction within a rather short exposure time (often 5 minutes). For instance in the Netherlands suspension tests are still the only mandatory tests in official regulatory procedures.

The surface tests developed by TC 216 are ‘tougher’ tests than suspension tests. Experience thus far indicate that concentrations/dilutions that pass the phase 2/step 1 (suspension) tests will induce a significantly lower kill (2-4 log reduction or even lower) in phase 2/step 2 (surface) tests. So much higher concentrations are needed in surface tests to obtain a similar reduction as in suspension tests. Concern has been expressed about increasing the in use concentrations to levels that are unnecessarily high; especially requirements for surfaces that are thoroughly cleaned before disinfection might be significantly lower than the 4 or 5 log reduction that is now required in the CEN phase 2/step 2 standards [17].

Ad (iii): This topic follows from the former. Probably the most important question is which collection of tests is required for the different label claims of disinfectant products. Therefore a special task group of TC 216 has...
drafted an ‘Application of Standards’ standard; the final version that is now in progress will become a proper guideline describing the relationship between the standards and the minimum required spectrum of activity for different applications [18].

From European to global harmonization

At the turn of the century, while CEN TC 216 slowly but steadily moved to its harvest season and Dr. Graziaella Orefici had taken over the chair from Prof. Reber, another organization took the initiative to explore the possibilities of a transatlantic harmonization of disinfectant testing, i.e. the Working Group on Pesticides of the OECD (Organization for Economic Cooperation and Development) within the context of its Biocides Programme. The objectives of this programme are: the development of guidance for efficacy testing and assessment and work towards harmonization of pass/fail criteria. This initiative coincided with a growing interest of the United States and Canada for the European quantitative approach of disinfectant testing and their growing criticism on the qualitative methods of the A.O.A.C.

To exchange views a Workshop was organized in April 2002 in Washington, with about 100 experts participating from research institutes, regulatory agencies and industry. With several colleagues from TC 216 I had the pleasure to be in the organizing committee of that workshop that focused on efficacy issues of antimicrobial biocides used on hard surfaces, porous surfaces or in water and materials treated with such biocides [19].

One of the items where consensus appeared to exist was the principle of quantitative testing of surface disinfectants under circumstances simulating practice. At present further initiatives are taken to compare the European Standards with the quantitative surface test developed in Canada (Dr. Satar).

Final remarks

Since 1970 we have witnessed in Europe an evolution from a huge variety of national test methods to a mutual exchange of views and collaboration that has resulted in general accepted European Standards for disinfectant testing. I feel privileged that I could contribute in this European harmonization process as delegate for the Netherlands. The Dutch are well known for their polder mentality, i.e. their preference for reconciliation of opposite views by reason. In this respect I really enjoyed the 13 years as a member of TC 216 and a variety of its working groups. In numerous meetings and social gatherings in so many interesting places - from Berlin to Paris, from London to Rome from Helsinki to Vienna and from Brussels to Zürich - national and traditional differences and controversies were discussed and solved.

Most important for me were not the details of the different methods but the open and honest discussions with so many colleagues, of which some became good friends. When I left TC 216 in October 2003 (due to retirement) I realized that its task was not yet finished and that the next generation has to consolidate and to extend what we have reached so far. Some colleagues have expressed concern about this future. I’m less pessimistic since nobody, neither manufacturers nor regulating authorities, can ignore the scientific knowledge that is condensed in these European Standards.

Curriculum Vitae

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Dr. B. van Klingeren has been working as a microbiologist at the National Institute of Health and the Environment in The Netherlands (RIVM) from 1966 till his retirement in 2003. For many years he was involved in research and assessment of new antibiotics and disinfectants. From 1990 till 2003 he represented the Dutch government in CEN/TC 216 ‘Disinfectants and Antiseptics’ and was a member of several working groups of this Technical Committee; moreover he was chairman of the Dutch Norm Committee on disinfectant testing, i.e. the national mirror group of TC 216, in that period. He has published several studies on the repeatability and reproducibility of quantitative suspension tests and a quantitative carrier test for the evaluation of disinfectants.

References

1. Mossel DAA. The rapid evaluation of disinfectants intended for food processing plants. Lab Pract. 1963;12:898-900.
2. Internationales Colloquium über die Wertbestimmung von Desinfektionsmitteln in Europa - 1970. Arch. für Hyg. u. Bakt. Sonderdruck 6/71, München-Berlin-Wien: Urban & Schwarzenberg; 1971.
3. The 2nd International Colloquium about the Evaluation of Disinfectants in Europe. Zbl Bakt Hyg I Abt Orig B. 1973;157:1-141.

4. Reybrouck G, van de Voorde H. The meaning of the results of four national disinfectant testing techniques. Zbl Bakt Hyg I Abt Orig B. 1975;160:441-55.

5. AFNOR. Association Française de Normalisation. Antiseptique et désinfectants utilisés à l'état liquide, miscible à l'eau et neutralisables. Détermination de l'activité bactéricide (méthode pour dilution-neutralisation). NFT 72-150. 1977.

6. Reybrouck G, Werner HP. Development of a new quantitative in vitro test for chemical disinfectants. Zbl Bakt Hyg I Abt Orig B. 1977;165:126-37.

7. Van Klingeren B, Leuissink AB, van Wijngaarden LJ. A collaborative study on the repeatability and the reproducibility of the Dutch standard-suspension-test for the evaluation of disinfectants. Zbl Bakt Hyg I Abt Orig B. 1977;164:521-48.

8. Arbeitstagung des erweiterten Europäischen Komites 'Zur Wertbestimmung von Desinfektionsmittel in Europa'. Zbl Bakt Hyg I Abt Ref. 1976;250:98-117.

9. Reybrouck G, Borneff J, van de Voorde H, Werner HP. A collaborative study on a new quantitative suspension test, the in vitro test, for the evaluation of the bactericidal activity of chemical disinfectants. Zbl Bakt Hyg I Abt Orig B. 1979;168:67-79.

10. Council of Europe. Test methods for the antimicrobial activity of disinfectants in food hygiene. Strasbourg. 1987.

11. Werner H-P, Borneff M, Borneff J. Development of a new test method for surface disinfection procedures. I. Communication: Literature survey with regard to the usual laboratory methods. Zbl Bakt Hyg I Abt Orig B. 1977;165:1.

12. Van Klingeren B. Experience with a quantitative carrier test for the evaluation of disinfectants. Zbl Bakt Hyg I Abt Orig B. 1978;167:514-27.

13. Reybrouck G. The assessment of the bactericidal activity of surface disinfectants. III. Practical tests for surface disinfection. Zbl Hyg. 1990;190:500-10.

14. Symposium Européen: Les Désinfectants. Organisé par le Laboratoire des Medicaments Vétérinaires CNEVA, Unité Antiseptiques-Désinfection. Fougères, 26 et 27 Septembre 1989.

15. Rotter ML, Koller WA. European test for the evaluation of the efficacy of procedures for the antiseptic handwash. Hyg Med. 1991;16:4-12.

16. Van Klingeren B. Disinfectant testing on surfaces. J Hosp Inf. 1995;30 (suppl):397-408.

17. Bloomfield SF, Arthur M, van Klingeren B, Pullen W, Holah JT, Elton R. An evaluation of the repeatability and reproducibility of a surface test for the activity of disinfectants. J Appl Bacteriol. 1994;76:86-94.

18. European Standard prEN 14885. Chemical disinfectants and antiseptics - Application of European standards for chemical disinfectants and antiseptics. CEN Brussels, February 2004.

19. OECD Workshop on Efficacy Issues of certain Biocidal Products 22-24 April 2002 Washington D.C. Summary Report, 15th October 2002 on website http://www.oecd.org/ dataoecd/28/7/2494153.pdf.

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