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Ms. Sipie Larkin
Mr. Stephen Zaluzny
MDP 122
Therapeutic Goods Administration
PO Box 100
Woden ACT 2606

28 April 2008

Re.: Invitation for public comment on the TGA's new regulatory framework for disinfectants.

Dear Ms. Larkin, dear Mr. Zaluzny,

I would like to submit some comments regarding the TGA's proposed changes to the regulatory requirements for hospital, household and commercial grade disinfectants. I am submitting these comments as a medical microbiologist with a particular interest in infection control, including an interest in antiseptics and disinfectants. My personal background is that I was originally trained in Hygiene and Medical Microbiology in Germany (University of Heidelberg), then worked for a period of time in the USA (Stanford University) and then moved to Australia, where I am currently working as a medical microbiologist at Flinders Medical Centre and Flinders University School of Medicine in Adelaide.

In my native Germany, antiseptics and disinfectants are tightly regulated by governmental bodies and by a professional Infection Control organisation (VAH; Verbund für angewandte Hygiene). There is a huge emphasis on antimicrobial activity of antiseptics and disinfectants, in other words, that they fulfil their purpose of killing or eliminating microorganisms most efficiently. Commercial products undergo testing according to European Union (EN series) antimicrobial testing standards. Tests from two independent laboratories (non-manufacturer-based) are required for an entry into a list of approved antiseptics and disinfectants ("VAH List"). Each list entry is valid for three years. Healthcare facilities (e.g. hospitals) use this list as a basis for purchasing antiseptics and disinfectants. The list has been in existence since 1959.

In the following appendix I will summarise the issues that are important from my point of view when it comes to antiseptic and disinfectant approval. These points come from (i) my everyday involvement in infection control issues as a microbiologist, (ii) my teaching at Medical School, and (iii) my insight into the German/European regulatory system. I would like to provide this as "food for thought", not as dedicated, concrete suggestions. I am certainly available for further discussions and am also attaching a series of supporting documents.

With my best regards,

A/Prof Matthias Maiwald

Submission regarding TGA's proposed changes to the regulatory requirements for hospital, household and commercial grade disinfectants

1. Nature of antiseptics and disinfectants

Antiseptics and disinfectants are chemical substances that exert non-specific killing action on various microorganisms. They are being used for inanimate objects, for human superficial skin or for mucous membranes. There is a wide range of substances and commercial products, and they generally differ in four aspects: (1) the spectrum of different microorganisms killed, (2) the types of clinical or medical applications that they can be used for (e.g. surfaces, instruments, human skin, etc.), (3) the overall antimicrobial activity or potency, and (4) the speed of action and whether the antimicrobial activity is immediate or sustained or both.

2. General requirements for antiseptics and disinfectants

There are two main requirements for antiseptics and disinfectants. First, they need to have excellent antimicrobial activity for the purpose that they are used for, and their antimicrobial spectrum must cover the common types of microorganisms encountered in the clinical situation that they are used for. Second, they must be safe in terms of potential adverse effects in the application that they are used for. For example, if a disinfectant is used on surfaces, it should not damage these types of surfaces that it is supposed to be used on. Also, it should not leave toxic residues on the surfaces that can come in contact with humans and it should not emit toxic vapours if people are present during the application. If it is an antiseptic to be used on human skin or mucous membranes, it should not damage these.

3. Potential adverse effects of antiseptic or disinfectant failure

Failure of antiseptics or disinfectants can have serious adverse effects. There is a potential for serious adverse effects from a safety aspect, such as when substances damage instruments or human skin or mucous membranes. The other area of serious adverse effects is in microbiological terms, when antiseptics or disinfectants fail to kill or eliminate the microorganisms that they are supposed to. This might lead to catastrophic healthcare-acquired infections in patients. One area of concern is instrument disinfection, e.g. if microorganisms are not eliminated from endoscopes, this can lead to infection with various blood-borne viruses or septicaemia with common bacteria. Another area lies in hand and skin antisepsis. If preoperative skin antisepsis fails to eliminate a significant number of microorganisms, this can lead to serious post-operative infections. If a hand antiseptic fails to eliminate microorganisms from hands sufficiently, this can lead to cross-transmission of nosocomial infections, even if healthcare staff are very observant in their hand hygiene practices. The latter scenario has been (unwillingly) underscored by a recent journal article (Rupp ME et al. Infect Control Hosp Epidemiol. 2008; 29: 8-15). The authors have introduced alcohol-based hand hygiene with a new product. Compliance with hand hygiene increased significantly compared with previous handwashing, however, nosocomial infection rates did not decrease, as would have been expected from the increased compliance. A closer look revealed that the authors used a commercial hand gel with only 62% ethanol, which by any standard has extremely minimal antimicrobial activity and cannot have passed stringent antimicrobial testing. The lack of antimicrobial activity is a possible and plausible reason why increased hand hygiene compliance might have failed to improve nosocomial infection rates (Maiwald M. Letter to the Editor. Infect Control Hosp Epidemiol. 2008; 29: 579-80).

4. Antimicrobial testing standards for antiseptics and disinfectants

Antiseptics and disinfectants require objective, reproducible laboratory testing to verify their antimicrobial spectrum and activity. These standards need to be different for each type of application that the substance is used for, e.g. surface disinfection, instrument disinfection, hand antisepsis, skin antisepsis, etc. The European Union, for example, has a comprehensive set of EN standards to assess the antimicrobial performance of antiseptics and disinfectants. One of the pioneers in setting up these EN standards is Professor Manfred Rotter from the University of Vienna in Austria, with whom I am in regular e-mail contact. For information, I have attached one of his articles on EN standards for hand antiseptics (Rotter ML. J Hosp Infect. 2004; 56, S6–S9).

5. Claims of manufacturers and errors in antimicrobial testing

Manufacturers of antiseptics and disinfectants are naturally biased towards their products. This is a normal consequence of advertising and of the desire for market share and profit. In addition, objective antimicrobial testing of antiseptics and disinfectants requires a great deal of microbiological expertise, and as a tendency, the results become better and more reproducible with increased experience in laboratory testing. The European experience, with which I am familiar, tells us that the healthcare community cannot and should not rely on claims as well as test

results supplied by the manufacturers. These problems are underscored by one recent example. I was visited by sales representatives of a company that markets an alcohol-based hand gel for use in Australian hospitals. That product has a large market share in Australian hospitals. It has been approved and registered by the TGA. From microbiological knowledge, judging the contents of the product, I could make a well-informed guess that the antimicrobial activity of this product is extremely minimal. The sales representatives claimed to me that the product passes EN 1500, which is a very stringent European standard for hand antiseptics. However, I looked up the literature and easily found two published articles that this product does not pass EN 1500. I e-mailed Professor Rotter, and the response was: (1) very few hand gels (as opposed to liquids) pass EN 1500, and the few that do generally contain significantly higher concentrations of alcohol, and (2) it is not uncommon that laboratories are inexperienced in antimicrobial testing and produce erroneous results.

6. Need of the healthcare community for information

The average healthcare worker is not familiar with the intricacies of antiseptics and disinfectants and their application. Also, professionals in the microbiology, infectious diseases and infection control communities are familiar with the broad context and many clinical applications of antiseptics and disinfectants, but are often lacking the knowledge of details that are necessary to judge and evaluate manufacturers' claims. As a consequence, manufacturers may succeed in marketing products with either insufficient antimicrobial activity or products that are not suitable for a particular purpose. For example, I have heard anecdotal reports that there are products that have been designed for community (household) purposes, but not for healthcare purposes, and some of these products are being marketed and sold in healthcare settings, because the information on the approval status is lacking (or not easy to obtain). As a consequence, there is a need for appropriate and comprehensive information from approval authorities to the healthcare community.

7. The Australian situation

I have not yet studied the Australian approval system in fine detail. But I gathered a few key elements of the Australian approval system. It appears that manufacturers submit their documentation, and the TGA evaluates the manufacturers' claims based on the documentation that they are submitting. There does not seem to be a set of Australian antimicrobial testing standards, and it appears that TGA is accepting results based on EN and US testing standards. Also, there does not seem to be a requirement for independent, non-manufacturer-based testing, and it appears that manufacturers' claims are only occasionally verified by independent testing, or when there are complaints or doubts about manufacturers' claims.

In addition, it appears that products can be searched on the TGA website and their approval status seen, but it appears that there is no comprehensive listing of TGA-approved antiseptics and disinfectants and the clinical applications that they are approved for. As a consequence for the Australian healthcare community, even for specialists in microbiology, infectious diseases and infection control, company representatives are often the first (and only) point of contact when it comes to purchasing decisions for antiseptics and disinfectants. If healthcare personnel involved in purchasing decisions are meticulous, the claims by the company representatives will then be verified by checking the approval status on the TGA website. But I am not sure if that happens as often as it should.

There is another aspect about Australian approval of antiseptics and disinfectants that I find intriguing. Very few people in the microbiology, infectious diseases and infection control professions that I have talked to know about what is involved in Australian antiseptic and disinfectant approval. But these are the very people that should know, because their professions involve dealing with the prevention of infections through antisepsis and disinfection. In stark contrast, almost everyone in the microbiology, infectious diseases and infection control professions in my native Germany knows in broad terms what is involved in approval in the German context. We learn this as part of our specialist training, and there is a great deal of awareness and discussion surrounding these issues. The reasons for the difference are not clear to me. But one possibility may be a lack of transparency of the Australian approval system.

8. The German approval system

In Germany, every antiseptic and disinfectant has to be registered with the federal Office of Medical Products (which is the equivalent of the TGA). In addition, the VAH (Verbund fuer Angewandte Hygiene) runs an approval and listing program. It was previously run by the DGHM (German Society for Hygiene and Microbiology). The features are as follows:

- The program has been in place since 1959.
- It employs stringent EN testing standards.
- Tests by two independent, non-manufacturer-based laboratories are required for list entry.
- A listing is valid for three years.

- The list contains over 800 different antiseptic and disinfectant products.
- There are different sections on different applications, e.g. surfaces, instruments, hands, skin, etc.
- All healthcare facilities (hospitals) are required to use only listed products.
- Conversely, hospitals can rely on the list for a comprehensive range of products with proven efficacy for their purchasing decisions, and there is no necessity to rely on information provided by company representatives.

There are similar lists in Austria and Switzerland. There is also an alternative, but very similar list in Germany, by the RKI (Robert Koch Institute, the Federal Health Office in Berlin). The RKI list is used in conjunction with antisepsis and disinfection when there is a public health issue (e.g. an epidemic).

Contact persons for the German VAH list are:

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I am sure these persons will be available for questions if details concerning the listing require discussion and clarification.

9. Summary: desirable features of approval

In summary of the above, I would like to identify the following three desirable features of an antiseptic and disinfectant approval process:

(1) Transparent approval process according to objective features and with antimicrobial activity as a main criterion.

(2) Requirement for independent, non-manufacturer-based antimicrobial testing according to stringent standards.

(3) Comprehensive public listing of approved products according to different clinical applications, as a purchasing guide for healthcare facilities.

10. List of supporting documents

Antisepsis180408bw3.pdf
Lecture that I am giving at Flinders University Medical School about antisepsis and disinfection.

VAHlisteVorwortEnglisch.pdf
Introduction to the VAH list in English.

Desmitliste2002DGHM.pdf
List of disinfectants by the VAH. This is the 2002 edition that was published when it was run by the DGHM.

Rotter2004.pdf
Paper by Professor Manfred Rotter about EN testing standards.

AustrianList20050104.pdf
Austrian list of disinfectants.

SwissListeDesinfekt.pdf
Swiss list of disinfectants.

RKIDisinfList1997.PDF
List of disinfectants by the Robert Koch Institute in Berlin.

HandAntimicrob171107a.pdf
Presentation about antimicrobial activity of hand antiseptics that I gave at the HICSIG meeting and Forbes Week in November 2007 in Melbourne.