

**AD HOC GROUP OF THE STATES PARTIES  
TO THE CONVENTION ON THE PROHIBITION  
OF THE DEVELOPMENT, PRODUCTION AND  
STOCKPILING OF BACTERIOLOGICAL  
(BIOLOGICAL) AND TOXIN WEAPONS  
AND ON THEIR DESTRUCTION**

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**Working paper submitted by Denmark, Finland, Iceland, Norway and Sweden**

**REPORT OF A TRIAL RANDOM VISIT TO A  
BIOPHARMACEUTICAL PRODUCTION FACILITY**

**INTRODUCTION AND OBJECTIVES OF THE VISIT**

1. The five Nordic countries Denmark, Finland, Iceland, Norway and Sweden have jointly carried out a trial random visit to a biopharmaceutical production facility. A medium-sized privately owned fermenter-based facility in Norway was visited in May 1998. The facility is part of a multinational corporation with production in several countries.
2. The Nordic countries are convinced that random visits are a necessary part of an effective compliance protocol, but also recognise that such visits have direct implications for the pharmaceutical industry.
3. The main purpose of the exercise was to evaluate the procedures for random visits, both as regards preparations and on-site activities, in cooperation with the facility visited, and to obtain sufficient information concerning the consistency of declarations, while taking due consideration of the need to protect Commercial Proprietary Information (CPI).

Further objectives were to assess the implications for industry and to evaluate whether the declaration formats need further refinement.

The exercise also provided an opportunity to inform the biopharmaceutical industry about the ongoing negotiations on a verification protocol to the BTWC and to enhance contact between national authorities and facilities which may be subject to random visits.

**IMPLEMENTATION OF THE VISIT**

4. The trial visit was carried out according to the procedures for a "random visit" described in the rolling text as issued after the ninth session of the Ad Hoc Group (5-23 January 1998). The declaration formats used were based on those from the eighth session of the Ad Hoc Group (15 September-3 October 1997). In the exercise the triggering function was the facility's fermentation plant and related activities.

(a) *Preparations by the Home Team and the facility*

5. Government representatives met with representatives of the facility to be visited four weeks before the visit took place. They explained the background for the visit, the mandate, the procedures, the role of the players in the exercise (the Home Team and the Visiting Team), "managed access", and the facility's right to protect CPI. The Home Team consisted of government representatives, technical experts and representatives of the facility.

The facility filled in the declaration forms after this meeting.

6. Before the visit took place the facility management circulated information on general procedures and the rights and obligations of the facility to its employees. Instructions were given on how to deal with questions from the Visiting Team.

(b) *Preparations by the Visiting Team*

7. The facility's declaration was circulated to the members of the Visiting Team two weeks before the visit. The Visiting Team had a short meeting the day before the visit started at which it reviewed the declaration and identified ambiguities.

8. The Visiting Team consisted of five persons from three different countries. Their professional backgrounds were applied microbiology (biodefence), process chemistry and pharmacology. Two members of the Visiting Team had experience in GMP (Good Manufacturing Practice).

(c) *Conduct of the visit*

9. Day 1: As part of the initial information given to the Visiting Team, the Home Team provided a briefing by representatives of the facility. The Visiting Team found this to be of a relatively general character. It included a historical overview, an organisational chart and a description of the facility's output and production processes. The Visiting Team was also informed about an incident which had occurred only hours before their arrival, involving a failed and subsequently discarded fermentation batch. The company stated that in accordance with corporate guidelines and the guidelines for the visit, no photography or sampling would be allowed during the visit.

The briefing was followed by a question and answer session. Questions asked by the Visiting Team dealt with the culture collection, medical records, ongoing research and development (R&D) projects, security procedures, and operating schedules for fermenters. The Home Team requested the Visiting Team to compile a written list of the documentation requested. The Visiting Team prepared an extensive list and also prepared an initial visit plan.

A tour of the facility was made in the afternoon. The Visiting Team visited the microbiological laboratories, some of the fermenters, the raw material storage, and one of the

R&D areas. During the tour, several interviews were held with employees, including the biomedical engineer responsible for the microbiological laboratories and the physician responsible for occupational health and safety. Before ending Day 1 of the visit, the Home Team and the Visiting Team met to review the facility's declaration once more. Most questions pertaining to the declaration were then resolved.

Day 2: The Visiting Team concentrated its work on the remaining questions relating to the declaration, which dealt particularly with the BL3 laboratory and the pilot plant used for R&D. The incident involving the failed and discarded fermentation batch was examined. A sample the facility had taken from the batch was studied by the Visiting Team.

The Visiting Team carried out additional interviews and was given access to some of the records it had requested. In cases where CPI concerns meant that access to certain information could not be granted, the Home Team made an effort to find other means of satisfying the Visiting Team's inquiries. Access to information in the form originally requested was limited, for instance, for staff medical records, R&D, and production input and output. As there are no requirements to record "non-use" of equipment, questions regarding this could not be answered comprehensively. However, the Visiting Team concluded that it had received satisfactory information.

10. In order to save time, the Visiting Team split into two groups on three occasions. This meant that one group could continue the main tasks, while a "satellite" group went to other parts of the facility for specific purposes, rejoining the rest of the Visiting Team afterwards.

11. Managed access was practised throughout the visit. Access to written information was strictly controlled, for example during the presentation of the batch runs for one fermenter and an R&D project. Members of the Visiting Team were accompanied by Home Team representatives whenever the Visiting Team left the room assigned to it. The Visiting Team was given access to most of the places it requested to see. When access was not permitted due to safety regulations and CPI concerns, the Home Team tried to accommodate the requests of the Visiting Team by providing alternative sources of information.

12. The facility invited representatives of the media to a press conference to inform about the purpose of the visit, and to avoid any possible negative publicity resulting from the distortion of facts or misunderstandings.

*(d) Special features of the visit*

13. During this exercise, there were no major cultural differences between the Home Team and the Visiting Team and no language problems (the exercise was conducted in English without any interpretation services or translation of documents required). The facility was accustomed to inspections of various kinds and could provide fairly well organised documentation. The visit was concluded well within the specified two-day limit.

## CONCLUSIONS AND LESSONS LEARNED

14. It was found that a random visit lasting two days:

- Gave sufficient time for the Visiting Team to carry out its work in accordance with the procedures and objectives of the visit; and
- Was an acceptable period of time for the facility inspected.

15. The facility visited considered that the visit had only limited and acceptable resource implications. Management costs were assessed as insignificant, given the likely scope, length and frequency of such visits.

16. Furthermore, the facility visited considered that the visit did not in any way interfere with or disrupt the daily production.

17. The facility was confident that CPI was adequately protected during the visit. The fact that the Home Team accompanied the Visiting Team throughout the visit contributed to this.

18. All questions relating to the facility's declaration were fully clarified. The Visiting Team found that the facility could account for all its declared activities and how production was conducted. However, the facility pointed out the need for further elaboration of the declaration formats. They could for example be improved by further specification and explanation of declaration triggers.

19. Although it was difficult to ascertain “non-use” of equipment, the visit clearly demonstrated that it is possible to obtain a credible picture of on-site activities at a facility by interviewing staff and reviewing records. The mere possibility of receiving a visit will therefore render it more difficult to use declared facilities for prohibited activities.

20. It was found to be possible in practice to account for non-production and idle equipment provided that facilities are required to keep records of this. The facility asserted that documentation recording “non-use” could have been kept and made available to the Visiting Team if the facility had been aware that such information would be requested. However, further consideration of how to account for the use of fermentation pilot plants without disclosing any confidential information on R&D is needed.

21. More specifically, the visit showed that:

- Visiting Teams can be fairly small and consist of 4 members who can split into two groups;

- The initial tour of the facility should preferably take place immediately after the introductory briefing by representatives of the facility. This would reduce the time needed for the Visiting Team to plan the visit and would make requests for some documents superfluous;

- The government representatives of the Home Team could have improved the smooth running of the visit by identifying areas of relevance to the Visiting Team to the representatives of the facility prior to the visit, and by ensuring that these areas were covered in the facility's introductory briefing. It would be of assistance to national authorities and facilities to include guidelines for facility briefings in the Protocol.

22. The visit contributed to confidence-building between national authorities and the facility.

23. Provided that the need for facilities to protect CPI is acknowledged, random visits will provide transparency and promote mutual confidence in a future verification protocol to the BTWC.

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