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**REPORT OF A JOINT UK/BRAZIL PRACTICE NON-CHALLENGE VISIT**

**Working paper submitted by Brazil and the United Kingdom of Great Britain and  
Northern Ireland**

**1. INTRODUCTION**

1. The United Kingdom and Brazil believe that non-challenge visits (NCVs) have a potentially significant contribution to make to a BTWC compliance protocol. Although the UK has conducted four practice challenge inspections, no practical work has yet been done on NCVs. Brazil believes that NCVs could provide a useful forum for addressing Article X cooperative questions. Brazil was also eager to gain practical experience of planning and conducting BTWC practice inspections. Accordingly the two sides agreed to hold a joint practice NCV.

2. The joint practice NCV had three main objectives:

- to examine the practicalities and issues involved in non-challenge visits, including the role of declarations;
- to test the utility of VEREX on-site measures with the exception of medical examination. Sampling and identification would only be performed if agreed and as appropriate;
- to explore opportunities to address Article X cooperation.

3. The practice NCV, including final preparatory work and end of exercise discussion, was held at the Institute Butantan, São Paulo between 11-14 March 1996. This site produces vaccines and sera. The role play element lasted two and a half days. This was divided into three parts, although there was some overlap between each of the phases: discussion of facility declaration; on-site activities; Article X cooperative aspects.

4. A mock site declaration was prepared and completed by the site before the inspection began. Guidelines for the conduct of the visit were based on those used and developed by the UK during its own national PCI programme. These also included a new section outlining the role of invited observers in an inspection/visit. A mock visit mandate was also provided for the inspection team (IT). This outlined tasks which could be carried out in a real NCV. A briefing paper on preparation for hosting and conducting inspections was provided to the Brazilian facility and government escorts - the Home Team (HT).

5. There were four inspectors, two each from the UK and Brazil with one of the UK visiting team members playing the role of team leader. The government "home team" consisted of one Brazilian (M.F.A.) and one UK scientist. There was one UK national and one Brazilian in the exercise control staff. In addition a representative of PAHO (Pan American Health Organization) acted as an observer. Only one senior member of staff from the Institute was engaged for most of the NCV. Other personnel, such as building managers and laboratory technicians, were involved as required.

6. The final morning was set aside for the NCV's Article X cooperative aspects. There was also some related discussion during the visit's on-site activity phase. The seminar took the form of a detailed presentation by a member of the IT (UK Health and Safety Executive, HSE) on health and safety matters, particularly the philosophy and implementation of biosafety regulations in the UK and European Union. Copies of several relevant guidelines and other publications were provided.

## **2. SUMMARY OF NCV ACTIVITIES**

7. The NCV began with a site briefing followed immediately by detailed discussion of the facility declaration. The IT sought clarification of several responses, particularly on the uses of animals, the description of one item of equipment, and the highest level of containment available.

8. The IT visited the following buildings: two of the main research buildings; the production buildings for aerobic and anaerobic vaccines; serum production and formulation/control and packing; and the animal house. The IT focussed on two vaccines: pertussis and tetanus, during which the HT provided a step-by-step description of the manufacturing process. The tetanus production records were also examined. Only the team leader and the Brazilian controller entered the pertussis manufacturing suite because of the vaccination and Good Manufacturing Practice (GMP) requirements. Other IT members remained outside, but were able to view the live area and ask questions about the equipment and waste handling processes.

9. In addition to the health and safety briefing, as part of the international cooperative aspects of the NCV, the site sought some technical advice on the proposed re-design of the area intended for the production and toxoiding of botulinum toxin. Site personnel were especially keen to know whether their re-design of the floor space, entry and exit points to the working areas were of an appropriately high safety standard for the biological materials that would be produced and processed. There was detailed discussion of the engineering drawing of the envisaged floor plan, followed by a visit to the proposed production area. During this

visit the plans were reviewed and the IT gave appropriate technical advice.

### **3. ISSUES**

#### **(a) The role of VEREX on-site measures**

10. The four main measures used by the IT were: visual observation; identification of key equipment; interviewing; and auditing. There were no occasions during the on-site activities when the IT considered sampling necessary or even desirable. However, the IT noted that tests and equipment used by the facility for quality control and assurance purposes could have been utilized if sampling had been performed.

11. Interviewing was the most important of the four measures, although all measures acted synergistically and interdependently during the NCV. There was only one formal interview when the Director of Production was invited to respond to questions on the facility declaration. At other times a series of question and answer sessions with individuals responsible for specific buildings or activities were held as the inspection team toured the site. This applied particularly during the discussion of the declaration and visits to the two vaccine production buildings. The quality and consistency of information provided and elicited by the IT was readily apparent giving a crucial insight into the nature, scale and scope of the site's activities and contributed to the IT's overall assessment of the site's functions.

12. During the visit to the tetanus vaccine production laboratories, the IT was able to establish that the process production records were comprehensive, readily understandable and easily accessible notwithstanding the language barrier. Had time permitted it would have been possible to establish and audit trail for particular production runs outlining everything from removal of master seed from the storage freezer, preparation, inoculation, production and down stream processing. Availability of such comprehensive records helped give assurance that the production equipment in this particular suite had been used for peaceful purposes.

13. Visual observation also played an important part - indeed it was responsible for identifying one of the discrepancies in the declaration when the team leader noticed the primate colony. Observing the layout and design of facilities and buildings provides invaluable insights into the site's capabilities.

#### **(b) The role of the declaration**

14. Completion of the declaration form was part of the NCV preparation and as such part of the overall exercise. To assist the IT's preparation a copy of the completed form was attached to the visit mandate. Overall there were few difficulties with the mock facility declaration form. The IT identified several ambiguities from the declaration before the on-site activities began. These were raised with the HT at the start of the NCV. One afternoon was devoted to discussion of the declaration. Although most questions were resolved in this opening session, further clarifications were provided later.

15. The declaration provided a backdrop to the on-site activities. The IT did not,

however, attempt to track down each and every item of equipment or to verify the declaration's quantitative statements. Instead the details were used to aid visits to key parts of the site, and to provide a basis for detailed questions about, for example, the origins, installation and use of specific equipment.

16. Two immediate lessons on the role of declarations are evident. First, all questions and terms used must be readily understandable to remove any possible cause of ambiguity, misunderstanding or grounds for omission. Second, it is essential to ensure that declaration returns cover all activities on the site and the best way to ensure that this occurs will be for all senior site personnel to contribute to the declaration's compilation.

17. The declaration might also include details of any issue on which the facility would like technical advice. However, this would need to avoid raising expectations that all issues identified would be addressed fully by the IT during a NCV. Moreover, the facility declaration should ideally be straightforward. It should not impose too great an administrative burden on those involved in its compilation.

**(c) Access**

18. Access to buildings, documentation or staff was not a problem at any stage. Constraints were placed on the numbers of inspectors given access in some areas. These were all linked to vaccination requirements. In production suites evidence of appropriate vaccination was required before access could be granted to individual team members. In two cases lack of immunization did not matter as the vaccine production areas could be clearly viewed from adjoining corridors. Protective clothing also had to be worn to conform with local manufacturing practice.

19. Time and team size were the principal rate limiting factors on the depth and degree of access into particular activities. With one and a half days set aside for on-site activities and a team of four inspectors, the IT could either focus on a single area or activity, or spread itself more thinly across a wider range of areas. In this case the IT visited several production and research buildings, but even with limited time it was still able to obtain a clear appreciation of the nature and character of the site's activities. One and a half days can offer a fair opportunity to conduct a cursory but careful site visit. This provides greater transparency and confidence than would otherwise be possible from scrutiny of a facility declaration.

**(d) Confidentiality**

20. Since the visited facility is a public institution, no major confidentiality concerns were raised. Only on two occasions did site personnel express concerns over a new purification process under development. The facility personnel believed the confidentiality concerns could be protected by managed access. Although access was provided to the equipment, no detailed explanation of the process was provided. However, there was neither requirement nor occasion for the IT to seek details. All the site's vaccines are bought by the National Ministry of Health for the national vaccination programme, and there were no sensitivities surrounding the scale, nature or costs of the production processes.

**(e) Compliance issues**

21. Although this exercise was a NCV rather than a challenge with a specific compliance concern under investigation, the IT was still tasked to keep the compliance aspect in mind. Nothing was seen or identified which could give any cause for suspicion: the openness and transparency from the site personnel provided a high level of confidence that the activities were as claimed notwithstanding the inherent BW production potential in the vaccine suites. The degree of access provided to all production areas, personnel and documentation enabled the IT to obtain a good understanding of the site's activities. It is worth noting that the measures used by the IT would also have been deployed had this visit been a challenge inspection. In essence the objective and tools remain the same regardless of the scenario: to obtain an understanding of the activities of the site through the combined use of the VEREX on-site measures.

22. NCVs are not intended to address specific BTWC compliance issues. They can only address compliance issues through transparency and openness. Several other aspects, however, might be seen as indirect benefits, such as enhancing any future Organization's knowledge of the functioning of facilities under different cultural backgrounds, their links with foreign institutions and other national organizations or companies. All of this information can contribute to country profiles and help build up BTWC awareness in States Parties.

**(f) Role of the Home Team**

23. Although the government Home Team (HT) did not have an opportunity to brief site personnel or tour the site ahead of the NCV, the pre-exercise meeting did give the HT an indication of the site's activities and allowed it to establish whether there would be any access problems. Therefore although the HT did not have the opportunity to meet and brief many of the staff, the pre-exercise meeting did in some respects serve the same purpose as the pre-inspection visit in the UK PCIs.

24. There was less call for frequent HT technical advice and assistance than during the UK's PCIs. This was largely because there were few commercial confidentiality concerns on this site. Consequentially there was less need for HT advice on managed access and on how to demonstrate compliance while protecting commercial proprietary information. The nature of the exercise, as a NCV, may also have contributed to this reduced need for advice from the government HT.

25. Despite these factors the HT did, particularly when the IT visited the vaccine production areas, take time to brief building personnel on the visit's purpose and what would be required immediately before the IT was permitted access. This advisory function, which only lasted about ten minutes in each area, helped ensure that the visit to the areas progressed smoothly by providing an opportunity to confirm that there were no access or confidentiality problems. This pre-briefing was also used to establish whether any particular local health and safety regulations needed to be taken into account.

26. Although the opening briefing within the exercise was short, the site provided very good briefings and documentation in the shape of the Institute's brochures and the Child Vaccine Initiative Mission Task Force report. The IT found these very useful as they provided clear and detailed information on the research and production programmes and the equipment present on the site. Such information and continued openness through the visit helped the IT fulfil its mandate. For this reason consideration of the content and presentation of briefings and documentation is an essential part of site preparation. The government HT can advise on the best format and content of such information packages. Briefing requirements and supporting documentation should all be identified before the NCV. Similarly any specific questions that the site management would like to raise under any cooperative element would also need to be identified and prepared in due time.

27. Following declaration of a site, Government advisers and site personnel should ideally make preparations for the possibility of a NCV. These could include drafting of guidelines on both the preparation for and conduct of a NCV; briefing of key site personnel on their role and contribution; identification of any potential problems over access to facilities or information and possible solutions; and preparation of specific questions for cooperation purposes. Upon notification of a NCV, the HT would check that preparations were adequate and that key personnel and relevant documentation were available.

#### **4. OVERVIEW OF NON-CHALLENGE VISITS**

##### **(a) General observations**

28. NCVs, as the first UK-Brazil joint exercise seems to indicate, are practicable and useful in addressing two interrelated objectives. Firstly, they may provide some reassurance of compliance, mainly through transparency and openness, by facilitating access to information that otherwise would not be available from the visited institutions' declaration, no matter how detailed and comprehensive. Secondly, NCVs can create a working environment that may be conducive to international cooperation in various fields, especially those that may have a direct bearing on the visited state's capacity to demonstrate compliance with the BTWC. A NCV can help determine whether the state can ensure adequate control over all relevant activities in the biological field on its territory or under its jurisdiction or control.

29. On this occasion the on-site activities did not pose any difficulties for the facility or its staff. All operated synergistically and to good effect. Although the time set aside for on-site activities amounted to only one and a half days the IT was able to visit a significant percentage of the production and research buildings.

##### **(b) Value of Visits**

30. Much depends on how such visits are viewed and what objectives are set for NCVs. However, given this exercise's parameters a considerable amount of information was still obtainable from "walking the ground". An opportunity to visit a facility, discuss its activities and functions with the personnel, and walk round both within and outside buildings provides a clearer insight into a facility's working procedures, capabilities and limitations than would

otherwise be available from a declaration form. They can make a significant contribution to transparency.

31. A site visit provides an opportunity to explore the relationship between the detailed information in the declaration form and the physical features and activities of the site itself. More importantly, it also gives a clearer insight into the nature of those activities and how and for what purpose various pieces of equipment have been used, are being used or might be used in the future. From all of this it is possible to derive some reassurance that the site and its activities are consistent with the Convention at the time of the visit.

32. A visit also offers opportunities to discuss Article X and international cooperation issues. Provided clear and limited objectives are set, then a NCV can serve as a forum for offering technical advice and information on issues of immediate interest and benefit to the facility.

33. Since NCVs are not driven by specific compliance concerns they can help create a frank interaction between the IT and the HT/site personnel. In such an atmosphere an exchange of information may be achievable, thereby making it possible to tackle compliance and cooperation aspects simultaneously. Indeed this exercise showed that clarification by site personnel, with a view to demonstrating compliance, can be complemented by technical advice from the IT to help identify possible improvements to site activities. Suitable international contacts on potential areas of cooperation could also be suggested. These contacts could be improved were there a section in the declaration form on: (i) areas of current cooperation between the institution and international organizations or countries; (ii) proposed or planned cooperative projects of programmes which were not in the end conducted, and (iii) areas of possible international cooperation within a future BTWC compliance protocol.

**(c) Limitation of Visits**

34. No prior assumption was made about the notification time for NCVs. It is recognized that the likelihood of detecting any potential violation of the Convention in a NCV is extremely remote. However, the fact that a site is going to be visited does offer some modicum of deterrence. The immediate constraints on a NCV, as exercised here, are essentially those of time and team size.

35. In the context of a NCV the utility of an exhaustive examination of the presence or absence of each and every piece of equipment or production activity reported in the facility declaration is highly dubious. There could conceivably have been time to check the consistency of statements in the quantitative ranges of the facility declaration, but this would have prevented other on-site activities. If time available for on-site activities is constrained, then objectives must be tailored accordingly.

**(d) Relationship between “compliance” and “cooperation”**

36. In this exercise there were no conflicts between the IT’s requirements to check for overall consistency with compliance and the cooperative aspects. As it transpired, the two

aspects were complementary. Time constraints on the cooperative elements within a NCV need to be kept in mind. Duplication of efforts by other international bodies, such as WHO or PAHO, could also run counter to cooperative activities within the BTWC framework. However, it is still necessary as part of other work on Article X to identify any gaps in the existing broad range of bilateral and multilateral assistance to see what might be done, for example, in the area of public health.

37. As long as there are clear boundaries between on-site activities and formal discussion of cooperative aspects, then there is no reason why NCVs should not address both issues. Indeed there may be occasions where there is a clear overlap and both cooperative and compliance aspects can complement each other during the course of on-site activities. However, there does first of all need to be a mutual recognition that this is indeed the case. As with the compliance elements of a NCV, there are clear limitations in what can be achieved in a short period of time. Precise and limited objectives must be established.

## **5. CONCLUSIONS**

38. A NCV offers an opportunity to discuss the declaration and to clarify and correct any omissions, inaccuracies or misunderstandings. The VEREX on-site measures were of considerable value and worked exceptionally well in combination. However, the use of sampling and identification, and medical examination, require further consideration. These might be much less intrusive if sampling and analysis were performed by site personnel under IT supervision and medical examination restricted to access to medical records with appropriate protection of individual identities. Continuous monitoring by instruments or personnel is not appropriate in a NCV.

39. Even with a short period of time available for on-site activities, it was still sufficient for the IT in this instance to acquire a much better appreciation of the nature and scope of the site's activities without detriment to any commercial concerns or undue inconvenience to the facility personnel. This achieved two things: first, it helped place the declaration into its proper context; and, second, the information acquired from both declaration and site visit together added significantly to transparency thereby increasing confidence that declared activities were what they claimed to be. As long as the objectives and expectations are kept within realistic bounds, and subject to the same limitations and assumptions used in this exercise, then NCVs could contribute significantly to an overall BTWC compliance regime.

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