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PHARMALab™

QUESTIONS AND ANSWERS

Rev01

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1. **In PharmaLab a Kinetic Reader?** Yes, PharmaLab has the capacity to take pictures throughout the incubation period and is able to show the evolution of the growth and to count colonies as soon as they appear.
2. **Do we need an initial validation?** PharmaLab is an automation of a compendial Method. Validation Rationale: USP40/NF35 General Notices 6 Testing Practices and Procedures provides guidance of the use of automated and alternative test methods. 6.20 Automated Procedures states “Automated and manual procedures employing the same basic chemistry are considered equivalent.” The statement is equally true for procedures employing the same basic microbiology such as a plate count and the Growth Direct™ System. Furthermore, 6.30 Alternative and Harmonized Methods and Procedures states “Alternative methods and/or procedures may be used if they have advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other specialized circumstances. Such alternative procedures and methods shall be validated as described in the USP40/NF35 general chapter Validation of Compendial Procedures <1225> and must be shown to give equivalent or better results.” However, the authors understand that the General Notices are being updated to be restated in terms of microbial methods as they are validated as described in <1223> Validation of Alternative Microbiological Methods not USP <1225>. USP40/NF35 <1223> also states the following "There are commercially available enhancements to growth-based methods that allow colonies on solid media to be read more quickly, with substantially less incubation time, than is possible using only the unaided eye. In the implementation of these enhanced methods for the detection of colony growth, only the detection capability of the method requires verification." This statement supports the view that the Growth Direct™ System is not an alternative method requiring method validation. Similarly, the PDA Technical Report No. 33 (Revised) dated September 2013, states the following: “Some alternative or rapid technologies may be considered automated traditional or compendial microbiological methods,

especially when the results are in colony-forming units (CFU). These technologies may be qualified for their intended use without the need for demonstrating certain method validation requirements as specified in Section 5.0 of the Technical Report. For these technologies, at least accuracy and precision assessments should be performed, in addition to method suitability and equivalence/comparability studies." The view expressed in USP <1223> was fully supported in this industry practice document. All analytical equipment, including that used for microbiological testing methods, is subject to industry-standard instrument qualification requirements. The revised chapter <1223> cites USP40/NF35 <1058> Analytical instrument qualification for general guidance in this area. This latter chapter includes the development of user requirement specifications and the well-known elements of equipment method qualification, installation qualification, operational qualification and performance qualification. The authors support the standard installation qualification (IQ), and operational qualification (OQ) approaches to the Growth Direct™ System but as outlined in the next section, not the standard performance qualification (PQ). A simple method verification approach would be substituted for the standard performance qualification approach.

3. **You mention the system is based on Artificial Intelligence does it mean that the SW uses the data acquired on the field to improve the algorithms?** In case of new features or updates, Copan will provide evidence of the evaluation of the impact of this change. Following the impact analysis, Copan will provide instructions/guidance regarding the necessity to repeat parts of IQ, OQ and/or PQ.
4. **What are the primary application fields?** Environmental Monitoring and Bioburden testing on the product or semi-finished, and process.
5. **Is real-time monitoring available?** Real-time Colony counting is available. PharmaLab can count colonies as soon as they appear. The system is also able to record and save the maximum number of CFU recognized.

6. **How the System manage the contamination risk?** Plates are not handled manually during the process and always kept closed during the analysis process. Moreover, PharmaLab is equipped with HEPA filters, that further decrease the possibility of external contamination.
7. **Can PharmaLab Manage double temperature?** Not in this moment in time. The choice to have only one temperature stems from the solution applied to avoid condensation. Both the incubator and the image analysis cabinet are set at the same temperature to avoid any temperature modification and prevent condensation. In this moment the technical feasibility for doble temperature is not available.
8. **Can you make only colony counting or do you have the morphology recognition as well?** Only colony counting in this moment. Morphology recognition is under development in our pipeline, and it is already applied in WaspLab, in the clinical field. The fact that our image analysis is performed with a standard camera (no fluorescence) enable us to develop the colony recognition.
9. **Is the system compatible with filters and grids?** Yes, the system has been tested and validated with white gridded membranes.
10. **What is the Plate Reading Technology?** System of HD cameras.
11. **Is the validation Book available?** It is available on customer request.
12. **Plate Dimensions compatible with PharmaLab?** Ø 60 mm, Ø 90 mm System tested with the major plate brands.
13. **Regulation Compliance?** We developed the system considering GAMP 5, and both European and US Pharmacopeia. Software is CFR21 Part 11 Compliant.
14. **What is the price?** Refer to Copan Sales in this moment.
15. **What is the delivery time?** 6 Months from PO.
16. **Installed base?** 0 equipment. 1 field validation in a Major Swiss Pharma.
17. **Equipment dimensions and weight?** 2.633 x 1.930 x 2.165 mm Weight: 1.450Kg.
18. **Maintenance service? Timing?** Software License + On-site assistance + Remote assistance via a secure network connection Provided by Copan or Local Partner.

Full-Service Package (Assistance); Annual preventive maintenance included; Full Life cycle management support.

19. **Is SW CFR 21 part 11 compliant?** Yes.
20. **Can we make the audit trail? Which characteristics?** Audit Trail is available. The instrument logs any action and associate it with the logged-in user (where relevant). Reports can be configurable.
21. **Time to read each single plate?** The system can read and analyse 120 plates/hour. It takes approx. 30s to perform the acquisition and analyse the pictures to give a number of CFUs.
22. **Number of pictures for every plate?** The total number of photos is 6 for every acquisition (3 different points of view X 2 light conditions). The system can take different pictures of the same plate during the incubation period.
23. **Is the system compatible with LIMS? Which type?** We can adjust our protocols to work with almost all the LIMS (leveraging on our experience with Cyclone + Wasp). This kind of configuration is something we agree before the installation with our SW department and end user's IT.
24. **Is the system compatible with Biotrend? Or compatible with any other Environmental Monitoring software?** Yes.
25. **How can we clean it?** The system is designed to be compatible with standard lab detergents except for NaClO based solutions. Always use non-abrasive, low-residue wipes, when carrying out he routinary cleaning. The system can be sanitized with Hydrogen peroxyde fog. There is a special device and procedure in place for this kind of activity.
26. **Do we need to install it in special locations?** No, the system can be installed in standard lab environment. Detailed specs are available upon request.
27. **Can we switch to one temperature to another one?** The temperature can be set from 20 to 40°C, and the system has the capacity to handle dual incubation, but using this strategy in routing can be complicated as it means you'll require one system per day of the week. This is because if the incubation protocol includes

dual temperature (e.g. 3 days at 22,5°C and 2 days at 32,5°C) the plates that enter the system on Monday need to change temperature on Wednesday, but the plates that should enter on Tuesday with same protocol should change temperature on Thursday and not on Wednesday.

28. **How can we manage the double incubation temperature?** See above answer.
29. **What is the stage of development?** The product is ready on the marked and validated to be installed at customer.
30. **What is the level of detection in terms of CFU detection and reading?** The system can detect a minimum of 1 CFU. It is impossible to provide a unique minimum dimension, given the numerous shapes, colours and morphologies in general of microorganisms.
31. **How many plates per day?** 120 acquisitions/hour -> 2280 acquisitions/day. Given an average capacity of the system of 2000 plates, and an average incubation period of 7 days, the system is designed to receive around 300 plates per day.
32. **Which is the maximum capacity?** The incubator can load up to 2.300 plates.
33. **Which type of media we can use?** The system has been trained with TSA, SDA and R2A (plus various neutralizers) from different brands. Any application that utilizes different media should be evaluated by Copan).
34. **Which type of plates we can use?** 90mm and 60mm lockable plates (the system is compatible with both formats at the same time).
35. **What is the capacity of the loading carousel?** max 370 plates.
36. **What is the time of reading?** 30s between one acquisition and the next one.
37. **Is the software able to manage labels / artefacts on the bottom of the plate?** Yes, it can manage labels on the bottom of the plate using the possibility of different light conditions from the bottom and the top.
38. **How does the SW for imaging acquisition work?** The image acquisition software prepares more than one picture to be analysed by the colony counting software using more than one point of view and more than one light condition.

39. **How does the SW for counting acquisition work?** The colony counting software is based on artificial intelligence and neural networks. The neural networks training is done before the software release to the customer so, once it is installed it is static. When a new version of the software with better accuracy will be released, it will be up to the customer to install this new version and to perform again the validation.
40. **Can we add more incubators?** In this moment in time, it is not possible to add more than one incubator to the same image acquisition cabinet.
41. **Number of plates in the incubator?** From 1.500 to 2.300 depending on plate mix.
42. **Is the validation available?** Validation book available on customer request. Copan will provide the specifications (electrical, mechanical, functional), the configuration, risk analysis and IQ OQ protocols. Additional document can be provided such as FAT and SAT protocols or internal testing reports. Copan can as well support end users with User requirement specifications and PQ protocol).
43. **Which suppot do you provide for validation?** See answer #42.
44. **Which are the main difference with the competition?** The main differences are: More capacity of the incubator. Open system (not propietary plates). Automation of compendial method.
45. **What can we export?** Pictures, reports, information regarding the incubation (e.g. loading time, id of the user who loaded the plate, acquisition time, temperature and humidity at acquisition time, manual counting results, id of the operator who did the counting, etc.).
46. **What the bar code import?** The barcode is scanned to retrieve information regarding the plate type (e.g. exact dimensions), to assure traceability inside the system, and to ask the LIMS the protocol to be applied to the plate (e.g. incubation temperature, duration of the incubation period, number of acquisitions, time of acquisitions).
47. **How big should be a colony to be read from the SW?** See answer #30.

48. **Temperature range and accuracy?** Customizable temperature setpoint (from 22.5°C to 32.5°C, adjustable on customer need) tolerance +/- 2.5°C. Incubator limits are 20-40°C.
49. **What can we change in the design?** The user can independently decide the mix of plates at the beginning of each cycle, using two different types of stackers (dedicated to 60mm or 90mm plates) for the input module. The incubator plates mix is defined together with the customer during installation, and any modifications must be carried out by Copan personnel.
50. **How complex is the validation?** The validation itself is not complex. It is a matter of comparing the output generated from the system and the manual results. For what regards the qualification of the incubator, it follows the standard practices.
51. **How robust is the validation performed?** The product validation has been performed on Copan laboratories and thanks to a field validation performed at customer premises (Major Swiss Pharma Company).
52. **Is PharmaLab able to detect artefacts?** Yes. The system has been trained to distinguish artefacts and colonies. it can read and detect only CFU during the growth.
53. **How PharmaLab manage the plate during the process?** Plates are loaded already closed and cannot be opened during the process but they will remain closed up to the end of the incubation reducing risk of cross contamination.
54. **Can you manage fingerprints on the plates?** Yes, they are managed as contact plates. Also, plates collected with active air sampling have the media surface not perfectly planar.
55. **Can you manage condensation?** Yes, the system has been trained to manage condensation. Plated are always kept at the same temperature during the process to reduce the problem. If the system detects condensation as cannot provide a reliable count of CFU, it will raise an alarm.
56. **Can you provide a global service?** In Europe we will serve the installations from Italy, or with qualified partners. In US Copan has a subsidiary (Copan Dx) with a

team of field service engineers. The same approach will be followed in APAC, where Copan is present with its facilities in China, Japan and, in the near future, in Vietnam.

57. **Any approval from regulatory bodies?** We opened the discussion; our strategy will be to submit some documentation to get suggestions and at the same time let them know about the technology. One more thing we are doing is get our quality system and lifecycle documentation audited by an independent consulting company with extensive experience in the pharma industry.
58. **Frequency of image acquisition?** The number depends on the protocol (you can customize it + it depends on the duration of the incubation) and on the saturation of the instrument. Given a throughput of 120 plates per hour, which means 30 seconds per plate, if for example there would be only one plate in the system it is possible to take a picture every 30 seconds. With a full incubator the frequency would be approx. 12 hours. That said, we do not think a higher frequency is really valuable because of the growth rate of microorganisms.
59. **Who stores the picture? How much space needed?** Pictures taken are available for storage. PharmaLab stores images only for a short period, the time necessary for the analysis. It is up to the end user to decide how many pics to store. We suggest keeping the first picture (T0), the last (Tf) and the one with the maximum number of colonies (Tmax).
60. **Why lockable plates only?** Now this constraint is due to the analysis applied. Our system uses the first picture to detect artefacts and discard them from the count. If the lid of the plate moves throughout the incubation the image will differ from T0 and the software will generate false positives.
61. **Which SW category from GAMP5 applies to PharmaLab?** Category 4, configured components.