



The Israel Chapter of PDA

העמותה לקידום המדע והטכנולוגיה הפרמצבטית בישראל

Report From Israel Chapter of PDA

Annual Meeting & Elections

24th December 2006, Tel Aviv, Israel

Over 250 members of the Israel Chapter met at the Dan Panorama for the eagerly awaited and popular Annual Meeting. Updates on chapter activities were followed by a series of fascinating lectures which are summarized below.

Organization of the event was as efficient as ever in the capable, professional and proficient hands of Amir Malka at BioForum.

Sigalit Portnoy, outgoing President, presented a summary of activities and addressed the large number of new members who have joined the Chapter during the past two years. Sigalit particularly emphasized the high quality of presentations, the scope and depth of professional knowledge and the readiness to share that knowledge within the chapter.

Thanks were expressed to the outgoing committee and particularly to Yaakov Adar for editing the newsletter.

Karin Baer presented the treasurer's report. This Chapter has more than 650 members after nine and half years activity. A breakdown of the budget was presented including fixed expenses and monies out versus input from events.

Dr. Miriam Kaplan of the Israeli Ministry of Health gave a presentation on Regulation from a Global Perspective. Referring to the EU initiative to draw in neighboring countries including those of the South Mediterranean (where lies Israel). Addressing international regulation, Dr Kaplan emphasized that where a country's pharmaceutical industry is in its early stages of development you will find different levels of compliance at different companies. Contract manufacturing usually drives GMP compliance upwards. Global harmonization is

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unlikely to be achieved in the near future. Israel is a small country with a huge pharmaceutical market. Resources are limited and there are no mutual recognition agreements in place although Israel has initiated processes both with PIC/S and the EU. Addressing the philosophy of regulation of a private sector such as the pharmaceutical industry Dr Kaplan questioned who is ultimately responsible for good or bad things that result in regulation of the industry? The Ministry has filled seven new positions in the past year which is a significant rise in resources.

Dr. Judith Aronhime from Teva pharmaceutical Industries provided a fascinating presentation on Polymorphism in the pharmaceutical industry. Dr Aronhime made a complex and much misunderstood topic appear simple and straightforward, using the popular example of chocolate which turns white and looks moldy when it undergoes transformation on aging to a different polymorphic form. Polymorphism is very common in pharmaceutical solids and polymorphs may possess different solid state properties: Melting point, solubility, hardness, density, thermal stability etc. Different polymorphs may have different pharmacological activity which can be disastrous. Identification of polymorphs uses: X-ray powder diffraction, for absolute identification of a particular polymorph: differential scanning calorimeter, FTIR/ Raman and solid state NMR are also used for research purposes. X-ray single crystal analysis is used to obtain a clear answer as to which hydrate/solvate you have.

Generation of polymorphs occur when different crystallization methods are used. (Solution, cooling regime, KMP, stirring etc). Control of crystallization parameters to consistently produce one polymorphic form is not always simple. Trace impurities, roughness of the vessel wall, seeds of stable forms floating in the atmosphere are but a few factors that may affect polymorphic form.



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Polymorphs differ in thermodynamic stability. Spontaneous transformations may occur for one state to another and is favored by exposure to solutions, light and mechanical stress.

Polymorphs are unpredictable as are their properties. There is a need to invest in process knowledge: to look for different polymorphic forms in the laboratory. The amount of knowledge depends on the amount of effort invested in looking for them. Change of Crystalline form may affect bioavailability e.g. Norvir (Ritonavir –Abbott) was withdrawn from the market because it failed a dissolution test after changing its polymorphic form.

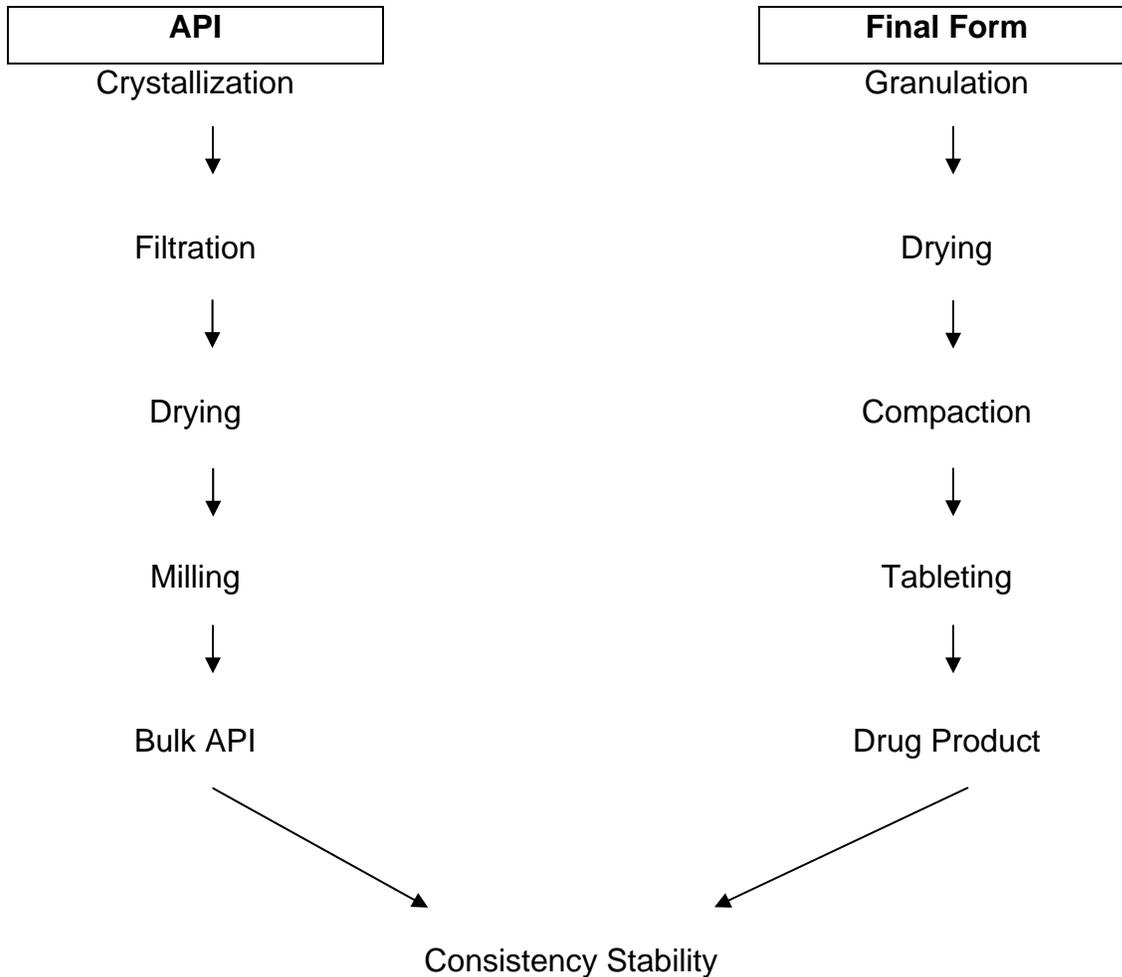


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Process steps to keep under control and product requirements

For each of the steps shown below, the question should be asked: “Are there polymorphs?”



Since it is permitted to register a patent on different polymorphic forms, generic manufacturers often produce different polymorphs and it is common to work with metastable forms. In this case process control is critical. In conclusion, Polymorphs are a case of “opportunity” versus “challenge.”

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Dr. Dudi Meraro of Taro discussed the use of Risk Assessment in microbiology. Dividing his presentation into four parts, Dr. Meraro addressed risk management in:

- (1) R&D: Quality of raw materials, packaging materials and closure system and Formulation: Characteristics of product that contribute to growth of micro organisms/ preservative efficacy system with case studies
- (2) Production: Critical systems, seasonal fluctuations, power outages and loss of pressures; Cleaning validation
- (3) Risk during product life cycle: Failure of preservative efficacy test, customer complaints, distribution chain
- (4) Changing production site, Quality Assurance/Quality Control investigations of objectionable organisms

Dr. Dror Wohlfeiler of Teva gave a presentation on Managing an efficient Quality Control Laboratory. Dr. Wohlfeiler addressed: Laboratory in the manufacturing process, Theory of Constraints and Analytical Compliance as well as Quality Control technologies and analytical services, Planning and Control, Purchasing as a separate activity for the laboratory and Technical and technological contents (IQ, OQ, Calibration). Of particular interest was the use of automated work centers and assessment of average cycle time – metrics as well as a computerized prioritization system.

The final presentation of the evening was made by Karen Ginsbury of PCI Pharmaceutical Consulting Israel Ltd. on the topic of FDA's recently issued Quality System Guidance. Karen compared the FDA approach with the existing European GMP guidelines that already address many of the items that appear in the new guidance. In particular, Karen mentioned Quality Management, job descriptions for personnel and evaluation activities such as auditing and quality metrics.



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Elections were held at the end of the evening and a new committee selected, details of which can be found on the Israel Chapter website.