J Pharm Innov (2012) 7:95–118
DOI 10.1007/s12247-012-9138-6

RESEARCH ARTICLE

Real-time Exceptional Events Management for a Partial Continuous Dry Granulation Line

Intan Munirah Hamdan · Gintaras V. Reklaitis · Venkat Venkatasubramanian

Published online: 20 November 2012

Abstract
Purpose This study focuses on the implementation of a real-time exceptional events management (EEM) framework on a pharmaceutical manufacturing process to demonstrate its efficacy in detecting, diagnosing, and mitigating incipient exceptional events on a continuous process.
Methods The real-time EEM framework integrates signed directed graph and trend analysis methods for diagnosis. Additionally, fast Fourier transform analyses are performed via a parallel moving window to detect oscillatory behavior. The EEM framework is demonstrated on a partial continuous dry granulation line consisting of two feeders, blender, and roller compactor and is shown to be capable of incipient fault diagnosis. In addition, simultaneous occurrences of different exceptional events are considered in this study, and a protocol is developed for multiple fault identification.
Results The framework is observed to detect, diagnose, and offer mitigation strategies within 10 s of event inception for the following cases: (1) simultaneous occurrences of different exceptional events in a particular, isolated, equipment, (2) simultaneous occurrences of different exceptional events spanning multiple equipment, and (3) consecutive occurrences of events. Additionally, the EEM framework is capable of limiting the progression of exceptional events originating in an upstream equipment, thus ensuring minimal to no propagation of exceptional events. Once an exceptional event has been determined, mitigation strategies are retrieved from the knowledge base and are either presented to the operator as an advisory or automatically executed to restore normal operating conditions.
Conclusions The real-time EEM framework is demonstrated to effectively detect, diagnose, and mitigate known exceptional events using built-in process knowledge. In addition, a protocol for handling multiple fault identification is successfully demonstrated on the partial continuous dry granulation line. Finally, quick and effective remediation of an exceptional event as it begins is shown to prevent the propagation of its effects downstream, thus reducing subsequent deviations across the continuous line.

Keywords Fault detection and diagnosis · Tablet manufacturing · Signed digraphs · Qualitative trend analysis · Supervisory control · Intelligent alarm management

I. M. Hamdan
The Dow Chemical Company,
2301 N Brazosport Blvd,
Freeport, TX 77541, USA

G. V. Reklaitis (✉)
Purdue University School of Chemical Engineering,
480 Stadium Mall Dr,
West Lafayette, IN 47907, USA
e-mail: reklaiti@purdue.edu

V. Venkatasubramanian
Columbia University Department of Chemical Engineering,
500 W 120th St,
New York, NY 10027, USA

Introduction

The development and manufacturing of pharmaceutical products have been governed by strict Food and Drug Administration (FDA) regulations which have been enacted to prevent potentially devastating consequences that could result should products not meet quality specifications. The same regulations, however, have impeded the use of systems engineering tools that could potentially improve the quality of products and the efficiency of operations. Fortunately, the pharmaceutical industry has been undergoing significant changes due to the advancement of the process analytical technology and quality by design initiatives by the FDA. It is evident that the industry as a whole is making concerted efforts to incorporate system engineering tools and practices that are prevalent in other industries in order to improve their manufacturing processes. Indeed, Suresh and Basu [1] have shown that investing in basic research in the science governing manufacturing and product development would result in reduction of new drug development costs and