AN AUTOMATED SYSTEM FOR NASAL SPRAY ANALYSES

Author: Herman Lam, Ph.D.
Manager, Automation & Lab Systems
Pharmaceutical Development Department, GlaxoSmithKline Inc. Canada

ABSTRACT

An automated system has been developed to determine the dosage weight and content uniformity of nasal spray products. The goals of the project were to prevent repetitive strain injuries, to improve test precision, and to increase the productivity in the lab. The system is designed to handle nasal spray containers of various sizes and shapes, as well as the variable dose collection requirements for the within bottle or batch content uniformity testing.

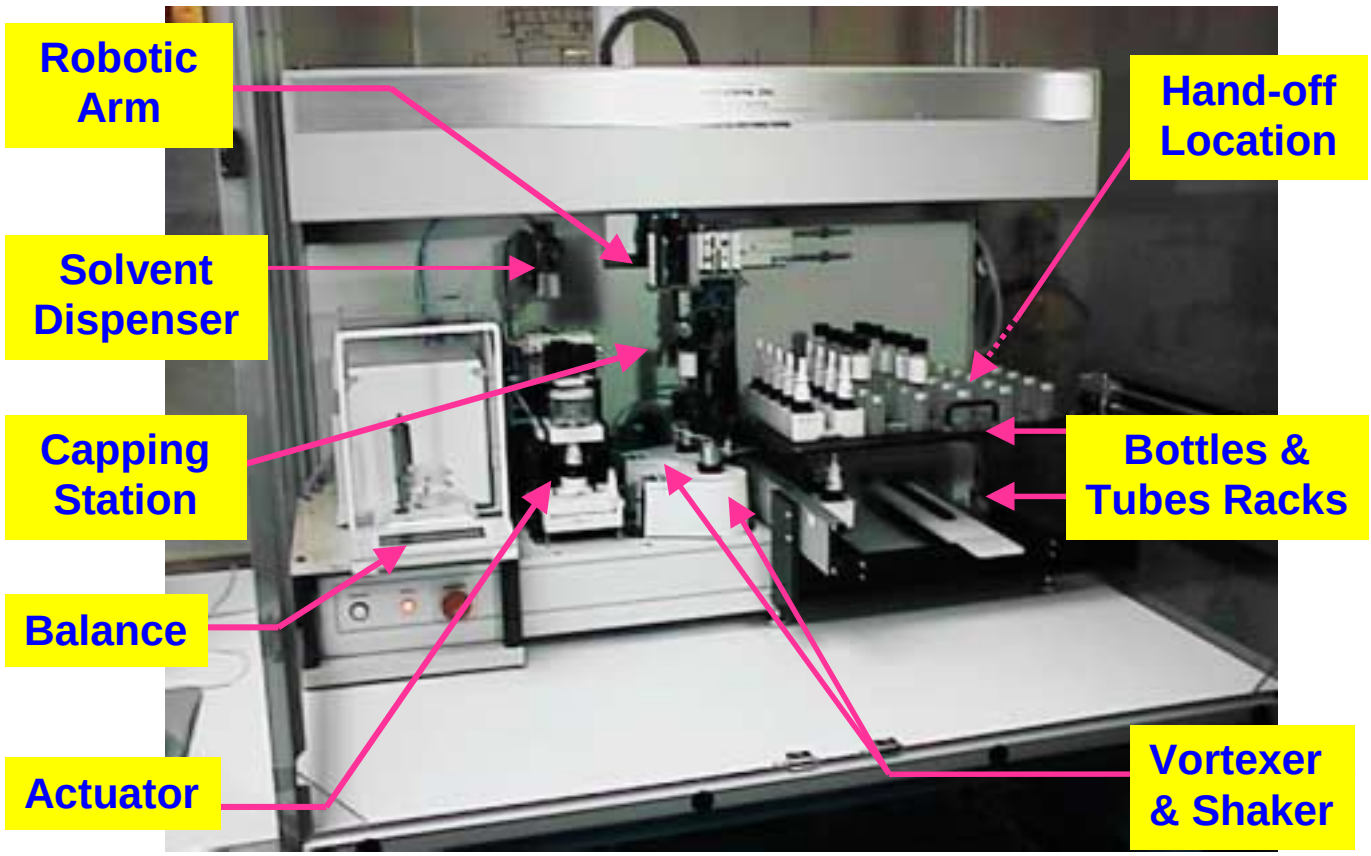
INTRODUCTION

Glaxo Wellcome Inc. (Canada) (GWI) is one of the primary manufacturing sites for two nasal spray products, Beconase AQ® Nasal Spray (BANS) and Flonase® Aqueous Nasal Spray (FANS). GWI is also heavily involved in the development of new nasal spray products. There is a big need to automate the labor intensive, manual testing methods for the testing of BANS and FANS and to facilitate new nasal spray products development. Automated testing will improve the efficiency and effectiveness of the testing process, improve the consistency of delivered dose test results, and address the repetitive stress health and safety issues of testing these products manually.

A nasal spray automation focus group was established within Glaxo Wellcome with worldwide representation from the primary manufacturing sites of nasal spray products. The focus group is co-chaired by representatives from Canada and Barnard Castle in the UK. The mandate of the group is to develop an automated nasal spray testing system that is suitable for worldwide use. InnovaSystems in Pennsaukens, NJ, USA was chosen to build a Nasal Spray Automated Dosage Delivery (NSADD) system (Figure 1) to automate nasal spray sampling. The design of the system is based on the user requirements and functional specifications developed by the nasal spray focus group. The NSADD system is capable of performing the following tasks:

1. Sample preparation for testing the Dosage Uniformity per bottle.
2. Sample preparation for testing the Dosage Uniformity per batch.
3. Dosage Collection and dosage weight determination.
4. Dosage Collection only.
5. Actuating a nasal spray bottle content to waste only, i.e., not collecting dosage samples.

Figure 1: Nasal Spray Automated Dosage Delivery (NSADD) System



NSADD SYSTEM OVERVIEW

The NSADD system has been designed to work with one type of nasal spray product at a time. The system may sequentially prepare samples or collect doses from up to 20 bottles from a single batch of product into a maximum of 60 dosage collection containers (sample tubes). The NSADD system was built around an actuator which is used to compress the nasal spray pump to deliver the samples to either the collection tubes or the waste container. The weights of the dispensed and collected dosage samples can be measured by the system. Also, analytical samples may be prepared from the collected dosage samples. These samples are stored in capped sample tubes for further processing and analysis. A Supervisory Control And Data Acquisition (SCADA) program controls the automated methods, collects the dosage sample weights, and records the status of the procedure and system throughout its unattended operation.

Hardware Description

The NSADD system is composed of two major hardware components: a robotic transport system and a bottle actuation, dosage collection and sample preparation station.

The "XYZ" robotic transport station will move bottles and sample tubes within the workbench space from station to station (Figures 2 to 6). A multi-purpose gripper is used to move both the nasal spray bottle by the bottle's nozzle tip and the sample collection tubes by the side of the tube (Figure 2a and 2b).

Figure 2a

Nasal Spray bottle in the gripper

Figure 2b

Sample collection tube in the gripper

The second major component is the Actuation/Collection station that actuates and collects the nasal spray dose into a sample collection tube or waste container. The actuation is achieved by compressing the nasal spray pump against a retaining metal plate (Figure 3a, b and c). The actuation force (in kilogram) and the speed (in seconds) can be adjusted for different nasal spray products.

Figure 3a: Actuation Station
Actuation to waste

Figure 3b: Actuation Station
Tube inversion

Figure 3c: Actuation Station
Dose collection

Other essential components of the workstation include an analytical balance, a bottle shaker, a capping substation, a solvent dispenser, and a sample collection tube vortexer.

The analytical balance is used to weigh the nasal spray bottles and sample collection tubes. Data collected from the weighing operations are stored in the system controller and recorded in a format that is suitable for importing into a spreadsheet (e.g., MS-Excel). The bottle shaker is used to provide a gentle shaking of the product between actuations to evenly distribute the suspension at the bottom of the bottle (Figure 4). The capping station will uncap the sample collection tube used to collect the dose sample, and cap the collection tube for vortexing and storage of the prepared samples (Figure 4).

Once a dose has been collected in a sample tube, solvent can be added to the tube in the solvent dispensing station. The sample tube vortexer is used to thoroughly mix the sample after the solvent has been added. During the dosage collection process, the “dabbing” station will be used to clean the nozzle tip of any nasal spray suspension residue (Figure 5). The robotic arm will pick up a bar of absorbing material wrapped around a Teflon core (the “dabbing” station) and gently touch the nozzle tip of the nasal spray bottle to remove any residue.

A double decker design is used to maximize the holding capacity for the nasal spray bottle and sample collection tube trays (Figure 6). Once the nasal spray bottles on the top tray have been processed, the top tray will slide forward to allow access to the samples on the bottom tray.

Figure 4

Capping and shaking stations

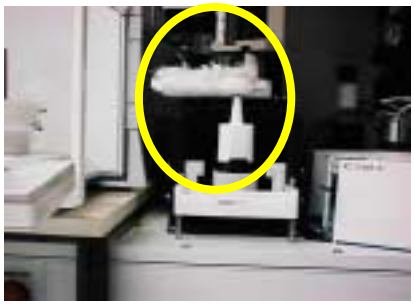


Figure 5

Dabbing action to clean the spray nozzle tip

Figure 6

Trays for nasal spray bottles and sample collection tubes

SOFTWARE DESCRIPTION

The system controller software is a Windows NT™ based, menu driven system that provides the ability to create methods, edit methods, view methods, run methods, run diagnostics, and run routines to validate hardware module functions. This controlling software will perform the tasks of steps sequencing, compiling, storing the method and product information, executing the programmed steps and collecting data. A Diagnostic module will allow the system operator to run routines that will test and troubleshoot the system hardware.

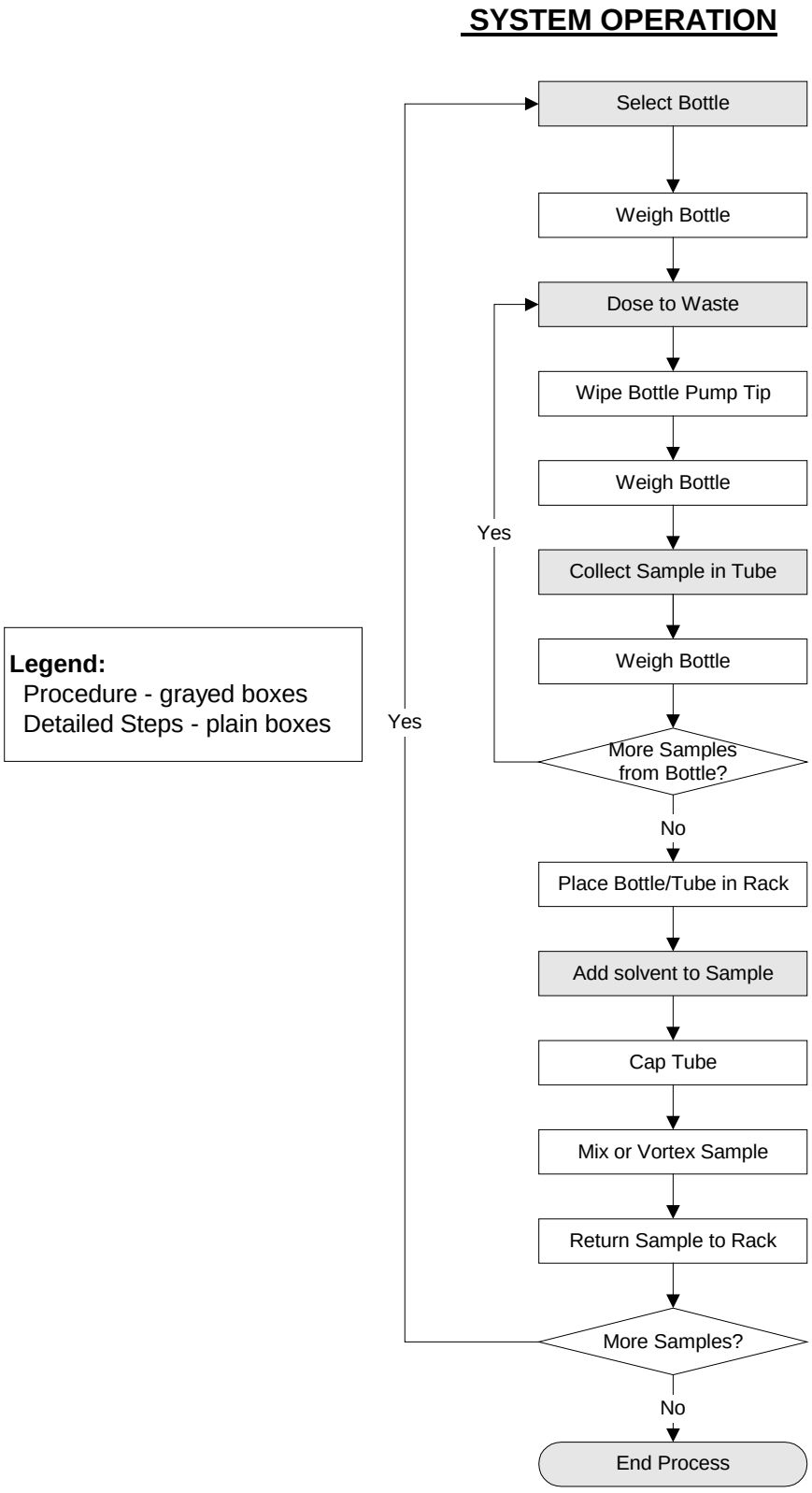
OPERATIONS

The NSADD system can be programmed to perform dose collection and sample preparation cycles that include dosage weighing, sample collection, or expelling doses to waste for each nasal spray container, as well as solvent dispensing and mixing to prepare a sample for analysis. A typical procedure for the dosage uniformity routines is shown in the flow chart in Figure 7.

The robotic arm picks up a nasal spray container from a holding rack and transports the container to the dose collection station. Several waste shots are fired to prime the dose delivery pump of the nasal spray container. A waste collector, which is a part of the dose collection station, collects the waste from the priming shots. Then, a dose collection tube is moved from the holding rack into position to collect the dose(s) that are to be analysed. The nasal spray pump tip is cleaned between collections by dabbing it with an absorbing material.

After dose collection, solvent is added to the dose collection tube. The tube is capped and the contents are mixed by vortexing. The tube is then returned to the holding rack. The cycle repeats according to the programmed sequence for the application. Both the weight of dose sprayed and collected may be obtained during the dosing cycle for each dose fired. The NSADD is capable of multi-tasking to shorten the cycle time required for each analysis.

Figure 7: Flow diagram of a typical content uniformity run.



DISCUSSION:

The NSADD is designed with the flexibility to analyse nasal spray products of various size and shape; as long as the spraying is actuated by a vertical compression force. The system can accommodate different nasal spray bottles by using boosters of different sizes and shapes to house the nasal spray in the actuation station. The gripping of the nasal spray bottle by the tips allows the robotic arm to transport the different kinds of nasal spray bottles without being restricted by the size and shape of the bottles.

The use of the collection tube may limit the number of doses to be collected. The tube can hold up to four shots without losing sample due to downward dripping. New regulations may require individual doses to be collected and analysed, so it is unlikely that each collection tube will hold more than two shots. However, if it is necessary to collect more than 4 shots into the same collection tube, modification of the tube may be required. One simple modification is to add a glass ring to the neck of the tube to collect the spray solution in the space between the wall of the tube and the ring (Figure 7).

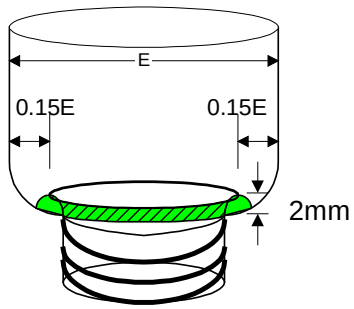


Figure 7: Modified collection tube for multi-shot collection

SUMMARY

A fully automated system has been designed and built to collect and prepare nasal spray doses for the BANS and FANS testing. By design, the system is flexible enough to accommodate nasal spray bottle of various size and shape. It is a valuable piece of equipment for nasal spray testing in both development and QC laboratories.

ACKNOWLEDGMENT

The author would like to thank Dr. Taryn Boivin for her enthusiastic support and encouragement in making the quantum transition from using off the shelf automated workstations to a custom built automated system. Dr. Bill Browett and Wilson Wong are the major driving forces in the project. Chantal Ravary contributed to the system qualification processes. Corinne Jackson provided quality assurance guidance to the project. Geoff Lloyd contributed significantly in the user requirement development and in the search of an engineering partner for the project. Also, the author wishes to thank InnovaSystems for providing the excellent engineering design and for building the NSADD system.