Photostability Comparison of the Drug Product Used for Reversal of Neuromuscular Blockade Caused by Rocuronium or Vecuronium and the Reference Product

Elif AKÇİL, Özden AKTAŞ, Dilan AKYOL, Sinem HASSAN BAŞARAN, Ebru İLHAN LALE
elif.akcil@abdiibrahim.com.tr
Abdi Ibrahim Pharmaceutical Company, AbdiBio Quality Control Department, Esenyurt, Istanbul, Turkey

Introduction

Photostability studies of drugs is an integral part of the product development process in the pharmaceutical industry. These studies are carried out to ensure quality, efficacy, and safety of the formulated products during manufacture, storage, and use.

ICH Q1B sets out the process by which we establish whether a drug product is photosensitive. Photostability problems can usually be addressed successfully by the selection of appropriate packaging: amber containers for liquid formulations, and opaque bottles or blister packs for oral solids.

Lux is the standard unit for illumination (the brightness of light as perceived by the human eye). Watt hours, as you might have guessed, is a measure of the amount of energy that the sample is exposed to which, as we've seen, is related to the wavelength distribution of the light source. So, the ICH guidance requires us to measure both the brightness and energy of the light to which the sample has been exposed.

Methods

The minimum light exposure levels in ICH Q1B need to be achieved:

•Illumination not less than 1.2 x 10^6 lux hours (equivalent to 2 to 3 days' exposure close to a sunny window in the summer)

•Integrated near UV energy (320 nm to 400 nm: UV A) not less than 200 watt hours per m^2 (equivalent to 1 to 2 days close to a sunny window)

One factor that we need to consider is the degradation that might occur in the photostability chamber independently of light exposure. For example, if the ambient temperature is too warm. To allow for this, we prepare dark control samples. These are identical to the exposed samples, but are protected from light, often by wrapping them in aluminium foil. They are placed in the photostability chamber at the same time as the exposed samples. If the impurity profiles of both dark control and exposed samples are the same, no photodegradation has taken place.

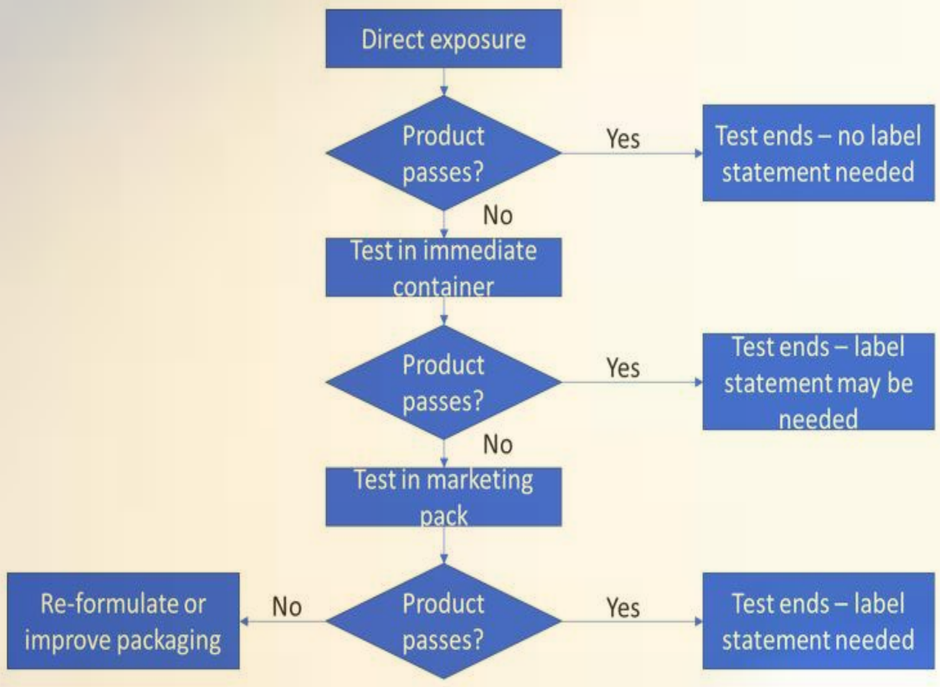


Figure.1: Drug product photostability decision tree

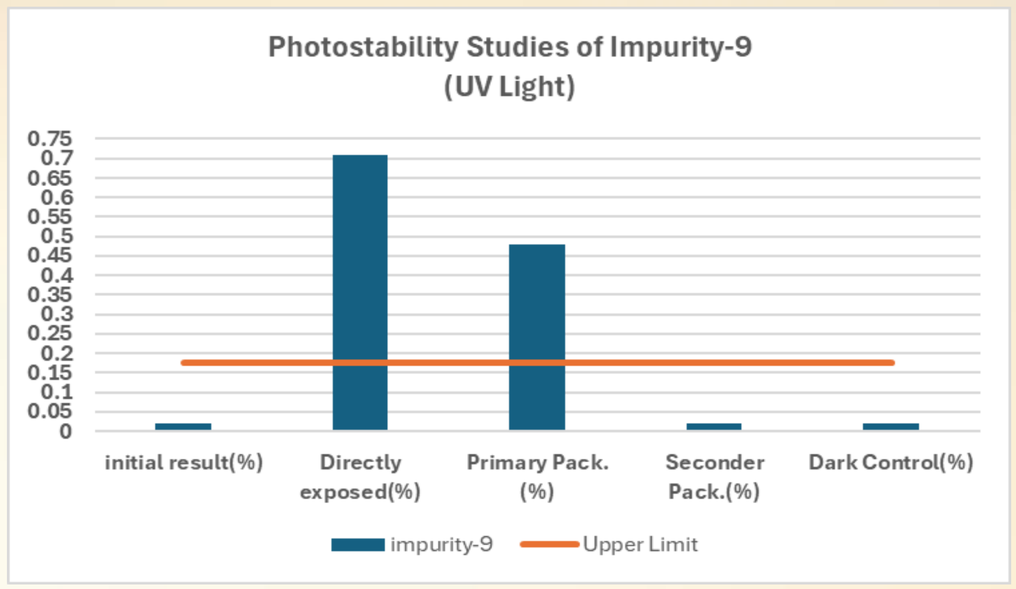
Results

UV Light (200 watt.h/m^2)

Control Parameters (UV Light)	Specifications	Fotostability Studies – Drug Product				
		Initials Results(%)	Directly Exposed (%)	Primer Pack. (%)	Seconder Pack.(%)	Dark Control(%)
Impurity-1	Max 1.0%	0.03<LOQ	0.03<LOQ	0.03 <LOQ	0.03 <LOQ	0.03<LOQ
Impurity-2	Max. 0.6 %	0.06	0.09	0.09	0.05	0.06
Impurity-3	Max. 0.6 %	0.08	0.11	0.10	0.07	0.08
Impurity-4	Max. 0.2 %	0.04	0.05	0.05	0.04	0.04
Impurity-5	Max. 0.04 %	0.02	0.02	0.02	0.02	0.02
Impurity-6	Max. 0.5 %	0.41	0.39	0.38	0.41	0.41
Impurity-7	Max. 0.2 %	N.D	N.D	N.D	N.D	N.D
Impurity-8	Max. 0.2 %	N.D	N.D	N.D	N.D	N.D
Impurity-9	Max. 0.175 %	0.02 <LOQ	**0.71**	**0.48**	0.02 <LOQ	0.02 <LOQ
Total Impurity	Max 2.5 %	0.60	1.48	1.22	0.60	0.60

Visible Light (1.2x10^6 lux.h)

Control Parameters (Visible Light)	Specifications	Fotostability Studies – Drug Product				
		Initials Results(%)	Directly Exposed (%)	Primer Pack. (%)	Seconder Pack.(%)	Dark Control(%)
Impurity-1	Max 1.0%	0.03<LOQ	0.03<LOQ	0.03 <LOQ	0.03 <LOQ	0.03<LOQ
Impurity-2	Max. 0.6 %	0.06	0.06	0.06	0.06	0.06
Impurity-3	Max. 0.6 %	0.08	0.08	0.08	0.08	0.08
Impurity-4	Max. 0.2 %	0.04	0.04	0.04	0.04	0.04
Impurity-5	Max. 0.04 %	0.02	0.02	0.02	0.02	0.02
Impurity-6	Max. 0.5 %	0.41	0.39	0.40	0.37	0.41
Impurity-7	Max. 0.2 %	N.D	N.D	N.D	N.D	N.D
Impurity-8	Max. 0.2 %	N.D	N.D	N.D	N.D	N.D
Impurity-9	Max. 0.175 %	0.02 <LOQ	0.14	0.13	0.02 <LOQ	0.02 <LOQ
Total Impurity	Max 2.5 %	0.60	0.74	0.74	0.57	0.60



Graphic.1: Drug product impurity-9 photostability results (UV light)

Conclusion

In the reference product instructions for use of our drug product, which is used to reverse the neuromuscular block caused by rocuronium or vecuronium, it is stated that **"Keep the vial in the outer carton in order to protect from light."** The stability products were exposed to both artificial daylight fluorescent lamp combining visible and ultraviolet (UV) light directly and also with their primary and secondary packaging in photostability cabinet. Based on the description in the reference product instructions, it was seen that the drug product was affected by light.

References

1) FDA,Q1B Photostability Testing of New Drug Substances and Products, **1996**
2) ICH, Photostability Testing of New Drug Substances and Products Comments for its Application
3) W Aman , K Thoma, "ICH guideline for photostability testing: aspects and directions for use", *Pharmazie,* **2003**, 58(12), 877-80.
4) Summary of Product Characteristics of Reference Product.