Uses of Capillary Electrophoresis for Pharmaceutical Quality Control in Japan

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CE in Japanese Pharmacopoeia

- Capillary electrophoresis procedures are described in General Information of JP (Japanese Pharmacopoeia).

- The pharmacopoeial texts can now be used interchangeably in ICH regions as the result of the Q4B process.

CE in Japanese Pharmacopoeia

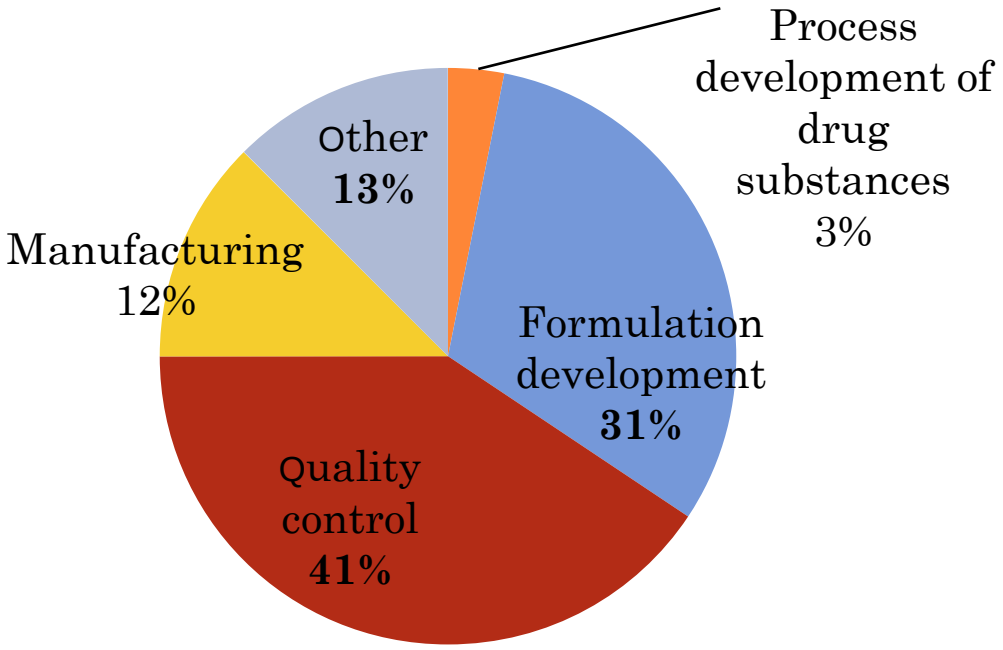
- General principles
- Apparatus
- 1.Capillary Zone Electrophoresis
- 2.Capillary Gel Electrophoresis
- 3.Capillary Isoelectric Focusing
- 4.Micellar Electrokinetic Chromatography

The use of capillary electrophoresis in Japan

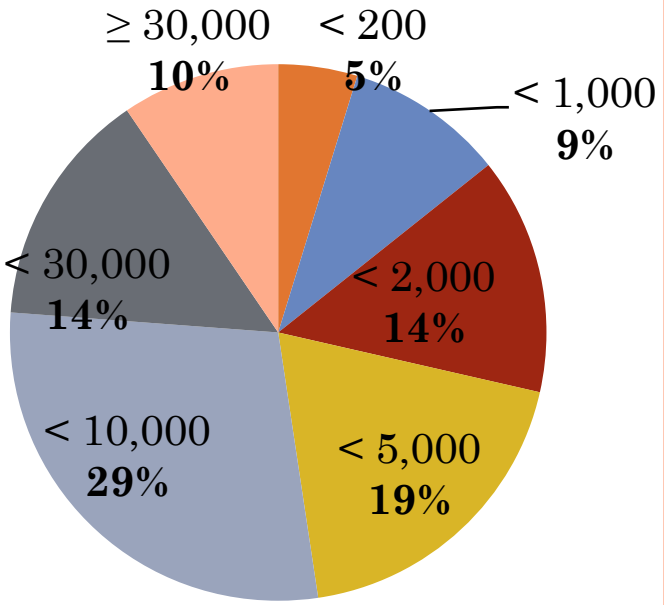
- Survey : how capillary electrophoresis is used for pharmaceutical quality control in pharmaceutical companies in Japan
- Members of The Japan Pharmaceutical Manufacturers Association (JPMA)
- **21 Companies, 32 respondents**

The use of capillary electrophoresis in Japan

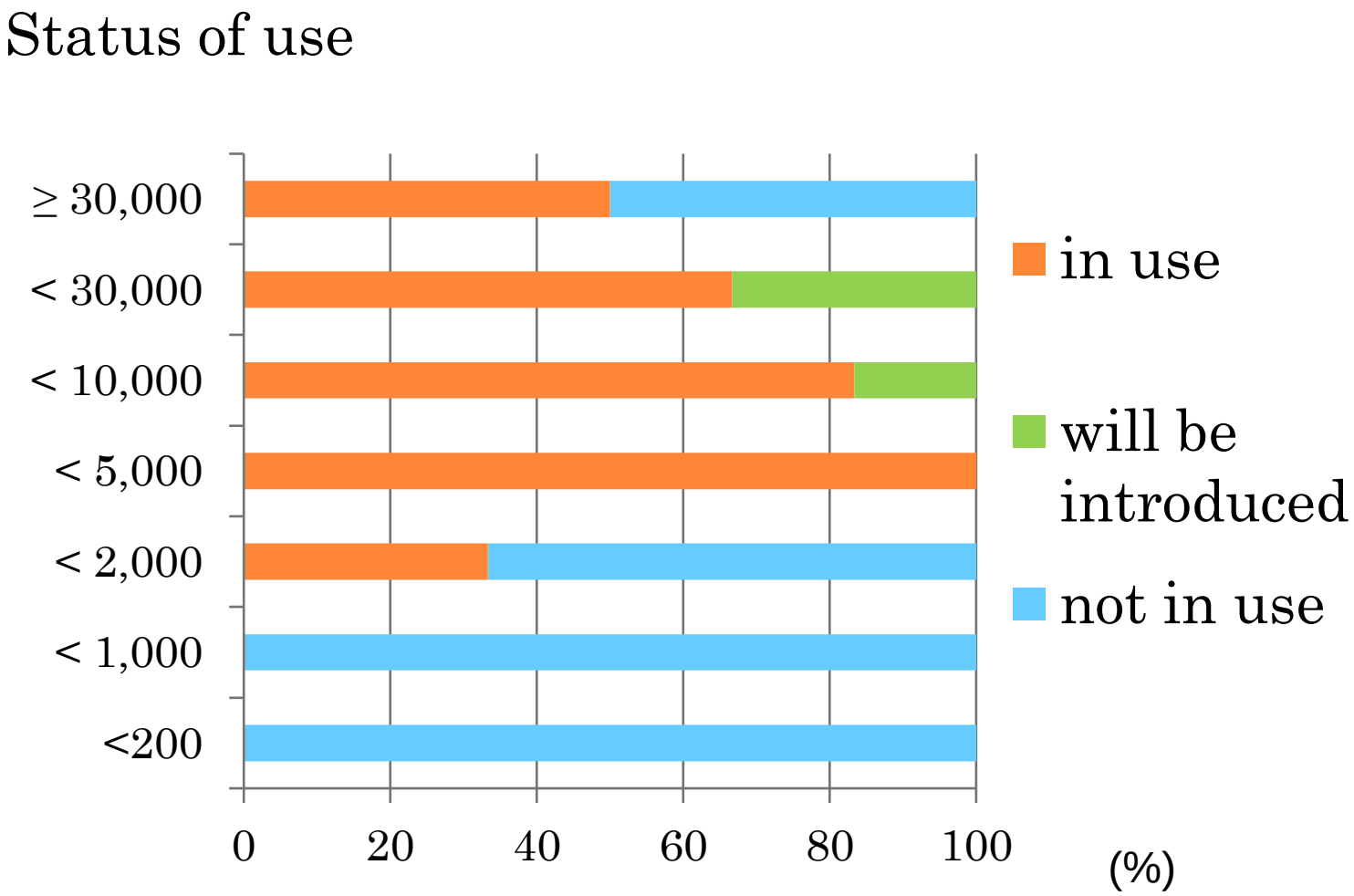
Target: Area



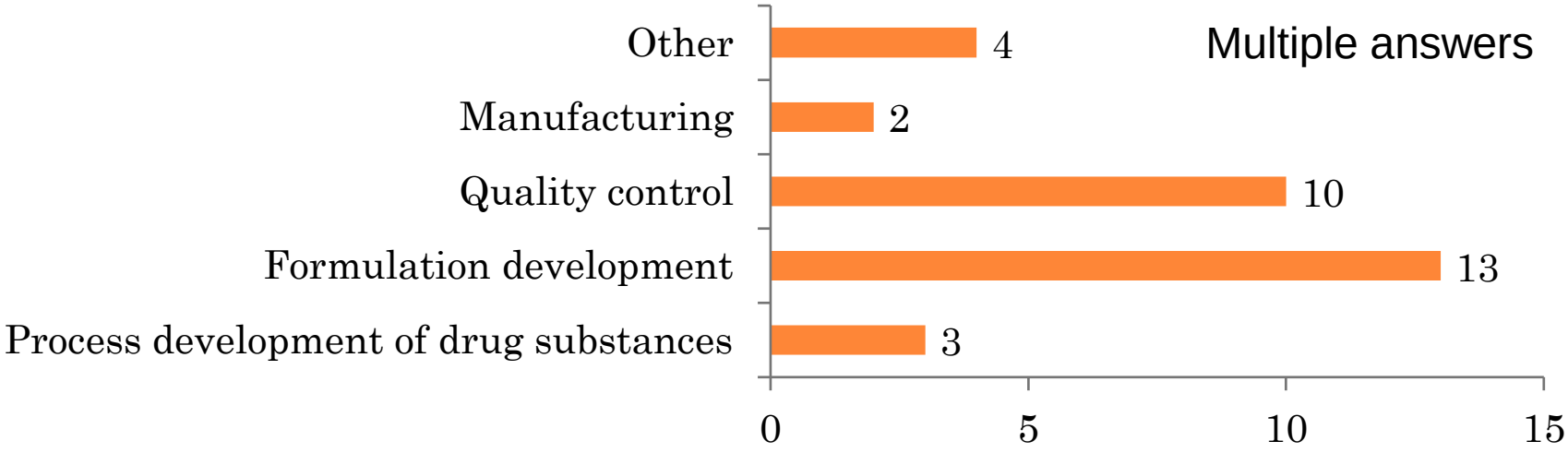
Scale of business



The use of capillary electrophoresis in Japan

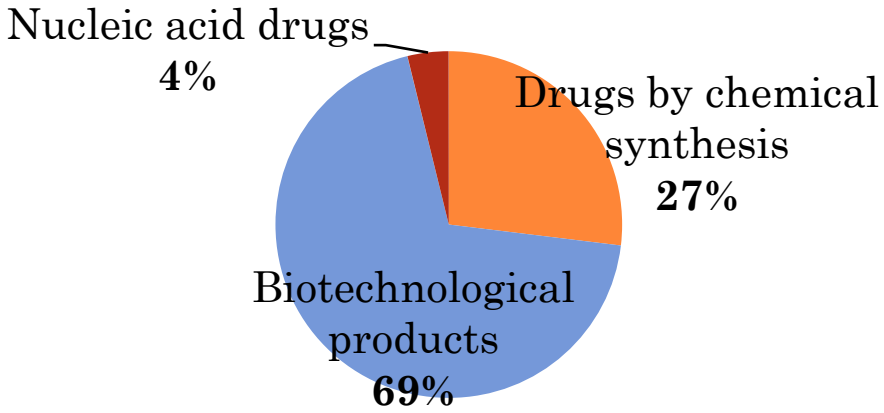


Area in use

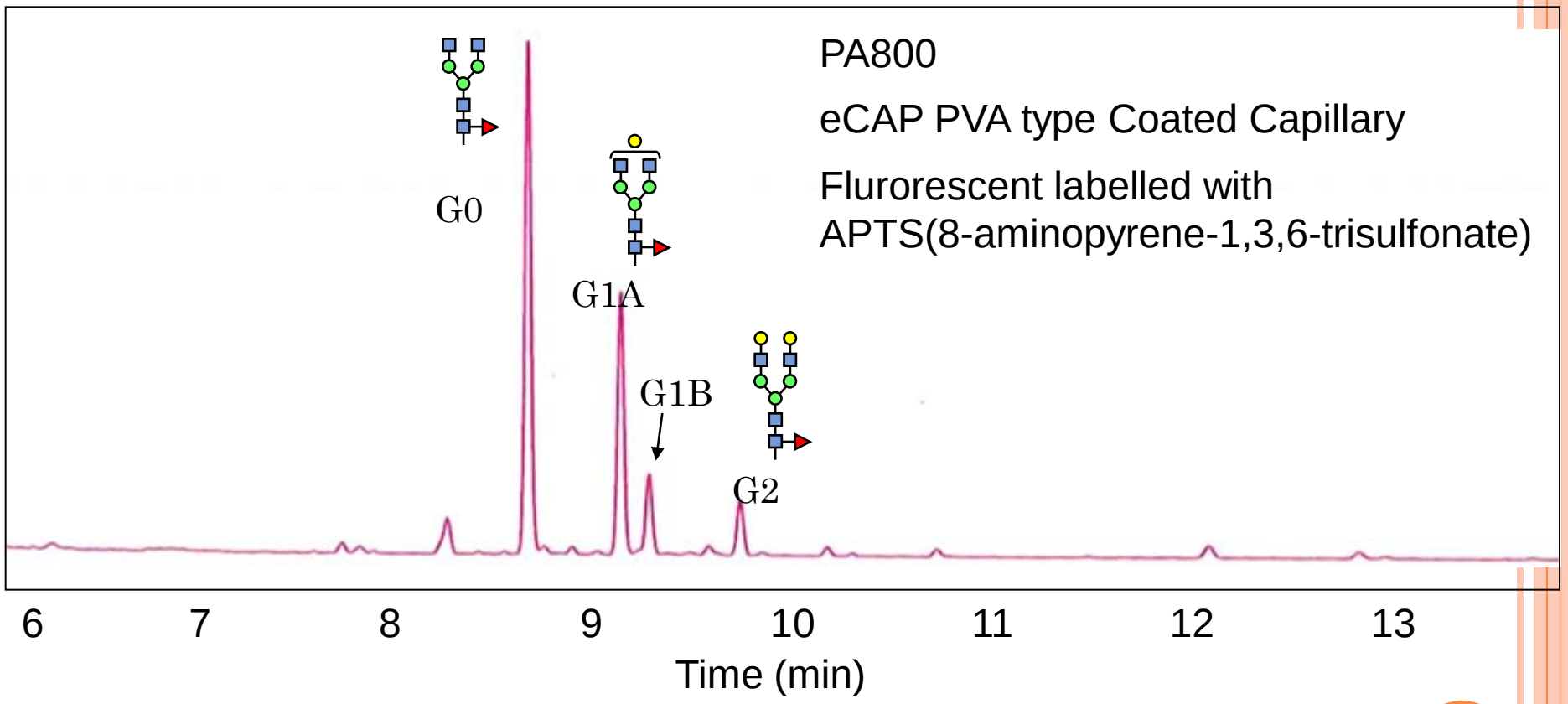


e.g.) Physicochemical properties of drug substances, specification, quality test (drug substances, drug products, excipients), stability test, monitoring for manufacturing method, shipping test

Target

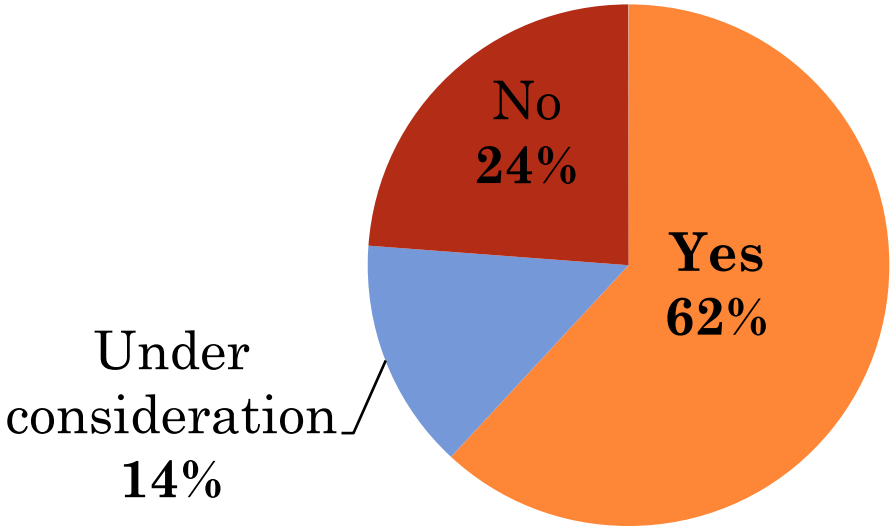


Example: Glycosylation Analysis of IgG



Courtesy of Dr. Nakashima (KAKETSUKEN)

Q. Has CE become part of the specification and test method ?



e.g.)

- Purity test (CE-SDS, c-IEF, glycosylation mapping)
- Identification test
- Process control of drug substances

ADVANTAGES AND DISADVANTAGES OF CE IN DRUG DEVELOPMENT

Advantages

- The variety of separation modes in the method.
- Quantitative performance, sensitivity, repeatability, automatization, short run time-compared to slab gel electrophoresis
- Small sample volumes, small effluent, characteristics of separation mode (e.g. ion analysis, charged compounds, highly polar compounds)

  -compared to LC
- The same software as for LC and GC
- Simultaneous analysis of various components

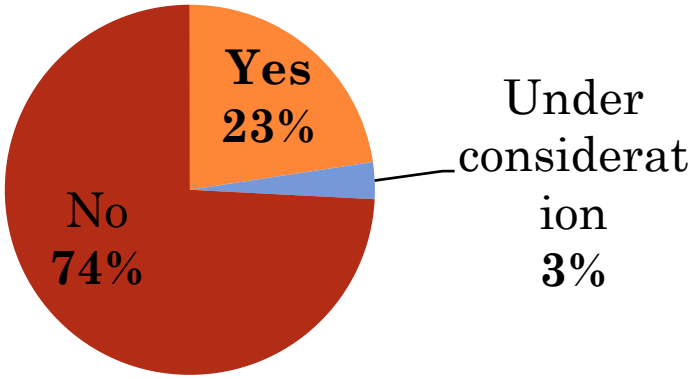
ADVANTAGES AND DISADVANTAGES OF CE IN DRUG DEVELOPMENT

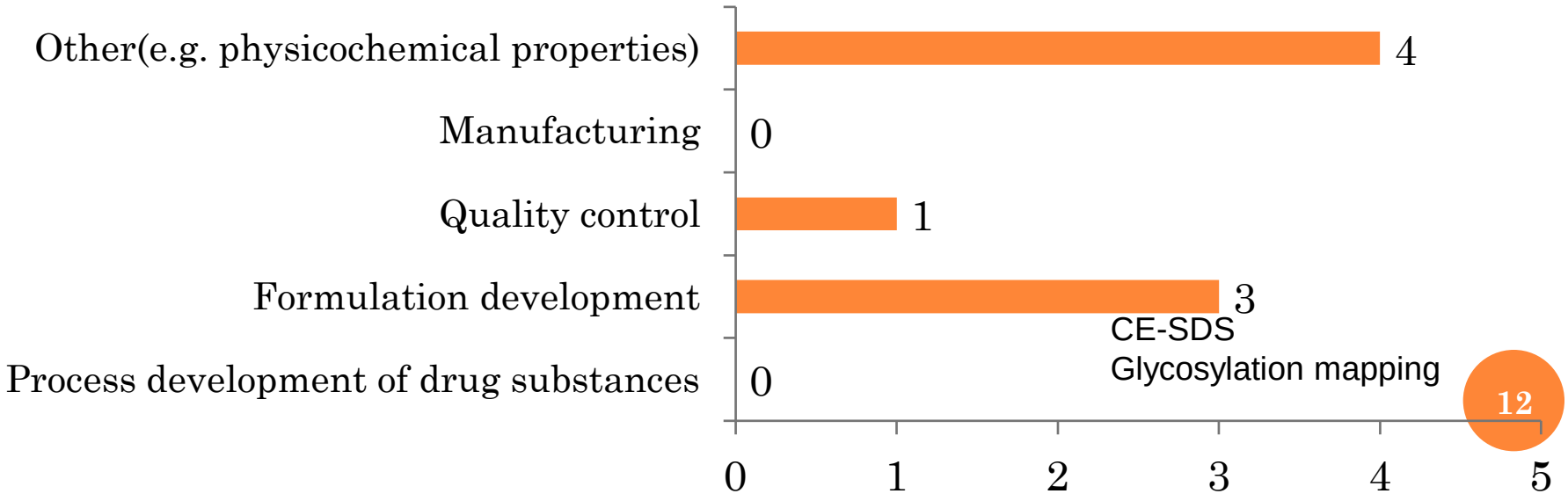
Disadvantages

- Not yet in common use, High cost
- Not repeatable (injection volume, eluent time, response, quantification), Difficulties in fractionation and low sensitivity –compared to LC
- Instability in performance (unexpected trouble, clogging of the capillary tube, difficulty in system conditioning)
- Difficulty in the setting of analytical conditions
- Difficulty in peak characterization
- Discrepancy of analytical results between different companies' instruments
- Matrix effect

The use of microchip electrophoresis in Japan

Status of use





General Comments from users

- CE will become a more important method if it is applied to more chemical synthesis drugs.

- Great skill is required to get data with good repeatability.

Requests to makers from users

- Devices to connect CE and MS
- Standardization of instrument specification between CE makers.
- Improvements in injection repeatability, automation of analytical optimization, and miniaturization of equipment
- Improvement of sudden instability in results
- Improvement of difficulties in injecting samples to equipment
- These improvements are necessary to enable an effective system suitability test.

Requests to regulators from users

- Standardization of method validation in purity test of therapeutic antibodies

  e.g.) - Accuracy of response factor for fluorescently-labeled antibodies

  - Robustness

- Standardization of injection method and washing method
- Standardization of method of calculating isoelectric point

Conclusion

- CE is an analytical method with many advantages such as quantitative performance, sensitivity, and short run time.
- However, there are some difficulties in the setting of analytical conditions, and peak characterization.
- By improving these difficulties, CE can be in more common use as methods for characterization, quality controls, and specification.

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Thank you for your attention!