regional assay laboratory was placed at a distance from the baby screening laboratory. In some instances, it will be necessary, as other screening procedures are developed, for the squares to be sent over greater distances to specialised laboratories. This punch took some time to develop because of the peculiar properties of the paper, which caused the difficulty in punching squares quickly from the Guthrie paper. It is a robust piece of apparatus and has proved acceptable to the operators.

We thank the Engineering Section of the Department of Anaesthetics for the use of their facilities.

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Letters to the Editors

Analytical goals in clinical biochemistry

In their paper 'A clinical view of analytical goals in clinical biochemistry' (*J Clin Pathol* 1979;32:893-6) Barrett *et al.* express the hope that their report will stimulate discussion. Having performed a study similar to the one described,^{1,2} I would like to enter this discussion.

They, like Skendzel,³ fail to recognise that there are two main—essentially different—areas of medical decision making:

- (a) the diagnosis—the physician has to distinguish the diseased individual from the normal population;
- (b) the follow-up of a patient—the physician considers subsequent laboratory results in one patient to follow the course of the disease.

If one studies desirable precision of laboratory results from the clinician's point of view by questioning the physician on the subject of a medically significant change in a patient (situation *b*), one has to be very careful in selecting the initial value. As I pointed out in response to Skendzel's paper,⁴ the physician's answers are bound to be ambiguous if the initial value is chosen within the normal range. Many physicians will indicate that the value passes a limit of normal or a limit of action rather than a change. In this situation it becomes irrelevant where in the normal range the initial value was chosen, and the difference between the initial value and the value compatible with a significant change is not necessarily indicative of desired precision.

This is the case for, for example,

calcium and cholesterol. Barrett *et al.* chose an initial value within the normal range, and the limit of normal (as apparent from my study) was given as an answer (Table 1).

I contend that the answers in the study of Barrett *et al.* would have been 2.66 mmol/l and 7.0 mmol/l for calcium and cholesterol, respectively, also when other starting values in the normal range had been chosen, for example, 2.55 mmol/l for calcium or 6.1 mmol/l for cholesterol, leading to entirely different conclusions with respect to desired precision.

In those cases where Barrett *et al.* chose an initial value outside the normal range the results correlate well with the results of my study where physicians were confronted with an initial value in the near abnormal range and were asked to indicate a medically significant change

(Table 2).

To determine desirable precision in the decision range between normal and just abnormal, the diagnostic situation (*a*) has to be considered and other criteria should be sought, such as, for example, the difference between limit of normal and the level prompting the physician to action.^{1,2} This is particularly important since clinicians appear to be more strict in the diagnostic situation.^{1,2}

There are a number of unwarranted or careless statements in the paper that appear to need reconsideration:

1 'This study is thus a baseline assessment of current clinical opinion for use in concurrent and future research.'

Irrespective of the question whether 62 physicians provide enough information to set such a baseline, the ambiguous set-up of the project interferes with the

Table 1

	Barrett <i>et al.</i>		Elion ¹
	Initial value	Medically significant change	Median limit of normal
Calcium (mmol/l)	2.60	2.66	2.67
Cholesterol (mmol/l)	6.5	7.0	7.1

Table 2

	Barrett <i>et al.</i>		Elion ¹	
	Initial value	Medically significant change	Initial value	Medically significant change
Sodium (mmol/l)	130	→	125	(5)
Potassium (mmol/l)	3.0	→	2.7	(0.3)
Chloride (mmol/l)	115	→	120	(5)
Urea (mmol/l)	9.0	→	11.4	(2.4)
			14.0	→
				11.5
				(2.5)

reliability of the thus established baseline. 2 'It is evident that the clinical view of analytical goals has not changed over the past decade.'

Barnett's 'medically significant values'⁵ are a 'synthesis of opinions of clinicians and laboratory specialists'. His paper does not state which questions were actually asked of participants in the study. Campbell and Owen⁶ 'presume clinicians have indicated acceptable analytical variability in the situation of a change in the normal range'. I disagree with the comparison of results of studies of ill-defined structure.

3 '... This may be because laboratories can indeed estimate plasma urea with less imprecision than plasma creatinine (...) and clinical opinion is very much influenced by actual present laboratory performance.'

No proof is given for the latter statement.

4 'The goals required ... are not as demanding as those promulgated by laboratory professionals.'

Barrett *et al.* fail to mention that the CAP goals⁷ are based on intraindividual variability. These are ultimate theoretical goals and are admitted to be 'possibly medically unrealistic'.

Finally, I would like to mention a confusing feature of the paper. Throughout the paper the terms 'required (desired) precision' and 'required (desired) imprecision' are both used, leading to expressions such as: '... laboratories can satisfy clinical criteria with regard to imprecision'. Comparably most girls in the beauty contest would satisfy the jury's criteria with regard to ugliness.⁸ The IFCC Expert Panel⁹ proposed the use of the term imprecision to describe analytical performance instead of precision since the measurable property of analytical variability, the SD, increases with increasing imprecision. They probably did not foresee the linguistic peculiarities that arise when these words are used indiscriminately.

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The authors reply as follows:

We thank Dr Elion-Gerritzen for entering the discussion on the derivation of analytical goals in clinical biochemistry, surely an area of the discipline of major importance. However, we believe some of the comments to be inappropriate.

It was indeed stated by us¹ that biochemical tests are used in many areas of medical practice, not only in two; for example, tests are used in aiding diagnosis, in assessment of prognosis, in monitoring treatment, in clinical emergencies, in research and development, and in screening programmes, but we believe that it is important to define numerical analytical goals and to apply a single numerical goal—the most stringent analytical goal—to all these different situations in order to facilitate discussions of topics such as errors with clinicians, and to ensure that emergency and routine diagnostic tests are totally comparable.

Dr Elion-Gerritzen is undoubtedly right when stating that the level of analyte chosen for survey is important, but the 'normal ranges' are not identical in all laboratories. For the two examples chosen by Dr Elion-Gerritzen, calcium and cholesterol, the calcium level surveyed, 2.60 mmol/l, is in fact slightly higher than the upper limit of the reference range of the Flinders Medical Centre (2.55 mmol/l), and the cholesterol level surveyed, 6.5 mmol/l, is used as the cut-off point for further investigation in our laboratory.²

We agree that the design of the studies of Barnett³ mpbell and and CaOwen⁴ are

rather different from that of the survey reported. However, we believe that comparison with previously published work, even though limited data are available, is of much value, and it is indeed usual for objective scientists to quote previously published relevant work.

The statement 'clinical opinion is very much influenced by actual present laboratory performance' is certainly empirical. It is, in our paper, prefaced by the phrase, 'This may be ...', and is therefore hypothesis on our part rather than statement of fact and was proposed as a factor worthy of future study.

It was indeed noted in the introduction to the paper that the CAP goals were based upon biological variation. We strongly disagree that these are the ultimate theoretical goals and can, like Dr Elion-Gerritzen, pick random phrases from the Aspen Conference Report⁵ to justify this statement, for example, 'the intent is to illustrate a quantitative approach to analytical goal definition' and 'the calculated analytical goal may be inaccurate'. However, these goals have, as stated by us, been widely promulgated and have been given approval by the Subcommittee on Analytical Goals in Clinical Chemistry of the World Association of Societies of Pathology.⁶ They are, therefore, the current goals deemed appropriate by the 'expert' professionals and should be noted in any publication concerning analytical goals.

The term precision was not used in our paper. The term imprecision is used throughout. The terms are not interchanged indiscriminately. Although there are semantic difficulties in using the term imprecision, we strongly believe that it would be desirable if all clinical biochemists conformed to the recommendations of the IFCC⁷ as confusion can be avoided by strict adherence to a single nomenclature system.

The study carried out was a baseline for our future studies. We, as stated, do recognise the deficiencies of clinician surveys and explained our views on the reasons for the poor response elicited.

We have not studied the work of Dr Elion-Gerritzen⁸ as it is not yet available in Australia. We look forward to the opportunity to comment, in an objective manner, on this work.

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